Annual Review

2024

Engineering and Physical Sciences Research Council

CMAC

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Introduction

Image: Prof Alastair Florence

Welcome to CMAC's 2024 Annual Report. The document gives an overview of CMAC's industry demand-led programme and highlights the fantastic outputs and progress made across the fantastic portfolio of funded projects delivered by the Centre's team. As in previous years, the report covers not only our research pillar and the major new initiatives but also our pillars for training and skills, facilities and translation to industry (T2I). Reading over the highlights, I hope you gain the strong sense of vision, common purpose and commitment the Centre and our partners have to working together to enable digital transformation of CMC processes and transforming the way medicines are developed and made.

The scope and scale of research touches on many critical areas to the industry. From accelerating development using material sparing, model-driven, self-driving DataFactories in the CMAC Hub and DM2 programmes, to enabling sustainable medicines manufacturing innovation in SolvIT and Net Zero to providing new structural insights on pharmaceutical materials in DDMAP, the innovative engineering and physical sciences research delivered by our researchers is creating the systems level framework necessary to support true transformation.

This year's report also covers the final phase of one of CMAC's flagship funded programmes in the EPSRC Continuous Manufacturing and Advanced Crystallisation Hub. This programme has been a tremendous success in delivering against CMAC's research strategy, with key outputs sharing: novel digital first approaches for continuous process design, novel mechanistic insights to particle engineering processes, digital workflows that establish a fundamental knowledge model describing key process development steps and a framework to enable the shift from Quality by Design (QbD) to Quality by Digital Design (QbDD).
https://doi.org/10.1016/j.ijpharm.2025.125625

However, we also look ahead with great excitement to the next phase of CMAC's development as a world leading centre for medicines manufacturing research. In October 2024 we launched the next phase of the Centre's critical mass programmes, built across three new major awards. This combines the UKRPIF funded CMAC Data Lab infrastructure programme, the EPSRC CEDAR Centre for Doctoral Training and the newly announced EPSRC Mediforge Industry 5.0 Manufacturing Hub for a Sustainable Future. Together these awards provide a world-class platform for the growing team of academics, researchers, PhDs and new and existing industry partners to develop innovative new cyber-physical systems and approaches that can help bring new medicines to patients sustainably, more cost effectively and at greater pace than ever before.

I hope therefore you find the report interesting and are inspired by the challenges being addressed and opportunities created across CMAC's rich portfolio. We very much look forward to hearing from you if you would like to find out more or discuss ways to get engaged. In the meantime, I would like to extend my sincere thanks to all of my colleagues, collaborators and partners who have been so generous with their ideas, time and commitment to make the Centre's ambitious precompetitive, multidisciplinary, collaborative programme a reality.

Prof Alastair Florence
CMAC Director

2024 Highlights

PEOPLE

150 People in CMAC

53 PhD Students

24 Management and Support

24 CMAC Academics

>55 Academic Collaborators

26 Research Staff

23 Technical Staff

6 Visiting Professors

DISSEMINATION

288 Papers across portfolio since 2017

126 CMAC Portfolio Technologies

314 314 attendees at online events

PUBLIC OUTREACH

170K Website users

5.6k followers - 40% increase on 2023

Outreach networks of **thousands**

46 Press releases since 2017

19 Schools visited since 2017

U3a: 2 events in **2024**

INDUSTRY

12 Industry visits

1 new CDMO member

New Translation to Industry Collaborator stream

STRATEGIC FUNDING & POLICY

£48.7m Industrial funding leveraged from Hub

46 Funding awards leveraged from Hub

9 Policy documents

Image: Tabletting

"2024 has been a transformative year for CMAC, defined by new collaborations and exceptional engagement from stakeholders and funding partners.

The invaluable support and strategic investments towards MediForge, CEDAR and RPIF Data Lab have fuelled CMAC's drive toward scientific advancements, strengthened translational capabilities, and deepened industrial collaboration to maximise impact.

These investments will continue to drive CMAC's enhanced translation capabilities, fostering impactful industrial partnerships, and opening new avenues of collaboration to address critical challenges in speed, complexity, digitalisation, regulatory, and sustainability."

CHARLES PAPAGEORGIOU
TAKEDA, AND CMAC INDUSTRY BOARD CHAIR

"CMAC has an unparalleled ability to deliver value to medicines manufacturing. Through its comprehensive research portfolio, state-of-the-art facilities and skills programme it's an invaluable centre for global and local companies to collaborate and innovate.

It's clear that CMAC delivers exceptional value to the industries it serves."

PROF. PAUL SHARRATT
SINGAPORE INSTITUTE OF TECHNOLOGY,
AND CHAIR OF CMAC ADVISORY BOARD

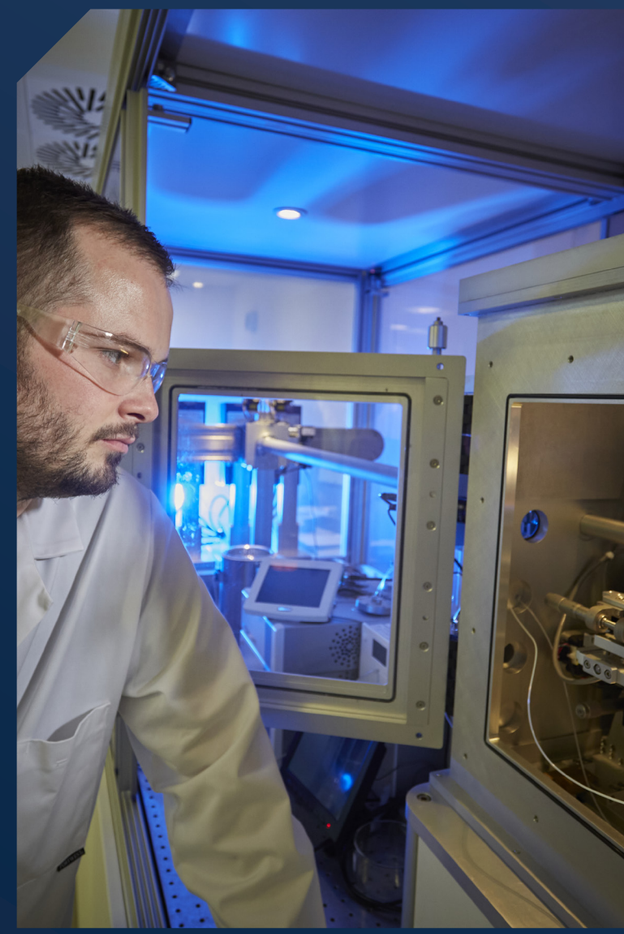


Image: Advanced charactersation

Vision, Mission & Strategic Priorities

VISION: To be a globally leading research centre to transform medicines development, manufacture & supply.

MISSION: To deliver value to our stakeholders by creating new science, innovative technologies and the future workforce that will support the adoption of advanced chemistry, manufacturing and control (CMC) development and manufacturing approaches to enable future drug substance, and drug supply.

Our activities are aligned to our four pillars:

Research Excellence & Intensity

Outstanding Skills Development

World Class Facilities

Exemplary Translation to Industry

CMAC is an **ambitious, people-oriented** organisation and our **inclusive and collaborative** approach to research is what informs our strategic priorities:

RESEARCH

Accelerate Development

CMC Digitalisation

Advanced Manufacture & Supply

Materials & Products

CENTRE

Lab of The Future

Future Workforce

Translation & Impact

World Leading Centre

Learn more about our VISION, MISSION, VALUES and STRATEGIC PRIORITIES at cmac.ac.uk

The Need for Medicines Manufacturing Research

MEETING THE GLOBAL CHALLENGE

The need to transform how we develop and manufacture medicines has never been more important if we are to address pandemic preparedness, supply chain resilience, the ageing population and the urgency for Net Zero. To realise the economic and social benefits from a robust, sustainable medicines manufacturing sector are required to rapidly translate breakthroughs in medical science to patient benefit.

To achieve this goal we must:

- Develop new science and engineering knowledge and translate it effectively to generate value
- Deliver digital transformation of CMC through industrial digital technologies
- Enable the deployment of advanced process technologies to support medicines development and manufacturing
- Create the skilled future workforce able to lead change

By working together to accelerate progress we can:

- Grow the vital medicines manufacturing sector
- Improve manufacturing productivity
- Reduce environmental impact
- Create wealth and jobs through new business models
- Support improved patient healthcare

Medicines manufacturing (MM) is a key sector for the UK, generating exports of over £25Bn with the highest GVA of any sector (£8.5Bn), investing over £4Bn p.a. on R&D in the UK. Globally, the medicine market is projected to grow at 3–6% CAGR over the next 4 years, with the total market reaching £1.2 trillion by 2025.

The Medicines Manufacturing Industry Partnership (MMIP) in the UK along with the US FDA have identified advanced manufacturing technologies including continuous manufacturing and industrial digital technologies (IDTs) as important solutions to these issues and assure cost effective, sustainable and secure access to quality medicines. The COVID-19 pandemic has also highlighted the need to invest in resilient, productive and flexible medicines manufacturing and supply chains. The climate crisis also presents a global challenge that is driving the international community to find ways to achieve Net Zero emissions and medicines manufacturing has to adapt to meet these goals head on.

DRIVERS & DELIVERABLES

Drivers for medicines manufacturing research

Accelerate pace of manufacturing innovation through understanding the needs of:

PATIENTS: rapid translation of medical science to benefit

INDUSTRY: provide access to medicines via secure supply chains

REGULATORS: guarantee patient safety

Targeting activities that will deliver the following benefits:

Collaboration is Key to Success

CMAC - CONNECTING ACADEMIC EXPERTISE WITH INDUSTRY NEED

CMAC aims to transform the current manufacturing process into the medicine supply chain of the future. Our collaborative approach brings together academic institutes, technology providers, global pharmaceutical companies and other key stakeholders to co-create and co-deliver transformative solutions.

ACADEMIC PARTNERS

University of Bath · University of Cambridge · University of Copenhagen · Ghent University · The Glasgow School of Art · Imperial College London · University of Leeds · Loughborough University · The University of Manchester · The University of Nottingham · University of Sheffield · University of Strathclyde Glasgow · UCL

TIER 1 PARTNERS

AstraZeneca · Chiesi · Lilly · Pfizer · Roche · sanofi · Takeda · UCB

TRANSLATION TO INDUSTRY COLLABORATORS

Ajinomoto · CCDC advancing structural science · digiM · Gericke · Lonza

TIER 2 MEMBERS & TECHNOLOGY PARTNERS

Applied Materials · Altair · analytik Laminar · Clairet Scientific Limited · Dec Group · element · syft Technologies · Fette Compacting · Huxley Bertram · KUKA · Malvern Panalytical · Medelpharm Instruments · M-Star · NVIDIA · SIEMENS · Snapdragon Chemistry · Technobis crystallization systems

THIRD SECTOR PARTNERS

A*STAR Institute of Chemical and Engineering Sciences · Cancer Research UK · Chemistry Growth Partnership · connected everything · cpi · diamond · UKRI Engineering and Physical Sciences Research Council · ICECUBES · Knowledge Centre Materials Chemistry · MHRA Regulating Medicines and Medical Devices · MMIP · NPL National Physical Laboratory · NHS Calderdale and Huddersfield NHS Foundation Trust · UKRI Research England · Scottish Funding Council Comhairle Maoineachaidh na h-Alba · Scottish Enterprise · UKRI UK Research and Innovation · The Wolfson Foundation

Innovation Landscape in the UK

Why?

Optimised pharmaceutical and high-value chemical manufacturing operations across the value chain which:

- Are economic, efficient, lean and world class
- Allows reduced time to market
- Are sustainable and wealth creating
- Deliver regulatory compliance

Benefits for patients

- Novel manufacturing technologies available
- Optimisation of processes that can be controlled or adapted

High value products resulting from

- Understanding of 'better and novel particles'
- Insight into particle formation
- Impact in formulation and quality attributes

High level impact of manufacturing research produced through

- Supportive governments
- Collaboration with companies
- Strong innovation network
- Strong UK Pharma base

Achieve in future

- Leading Tier 1 and supply chain partners
- Talent pipeline of of PhD, MSc and post docs
- Impact of technology on new medicines and manufacturing
- Process development using grams of material through Quality by Digital Design
- Grow world-leading pre-competitive research programme
- Improved manufacturing process and quality will benefit patients and producers driving CMAC's sustainability
- Create facilities to enable innovation, and enhance process development to support manufacturing
- Focus on manufacturing translation will cement CMAC standing as leading International Centre influencing policy
- Production of MicroFactories will enable future pharmaceutical manufacturing and create jobs
- CMAC research impacts to save time, capital and de-risk investment for pharmaceutical companies

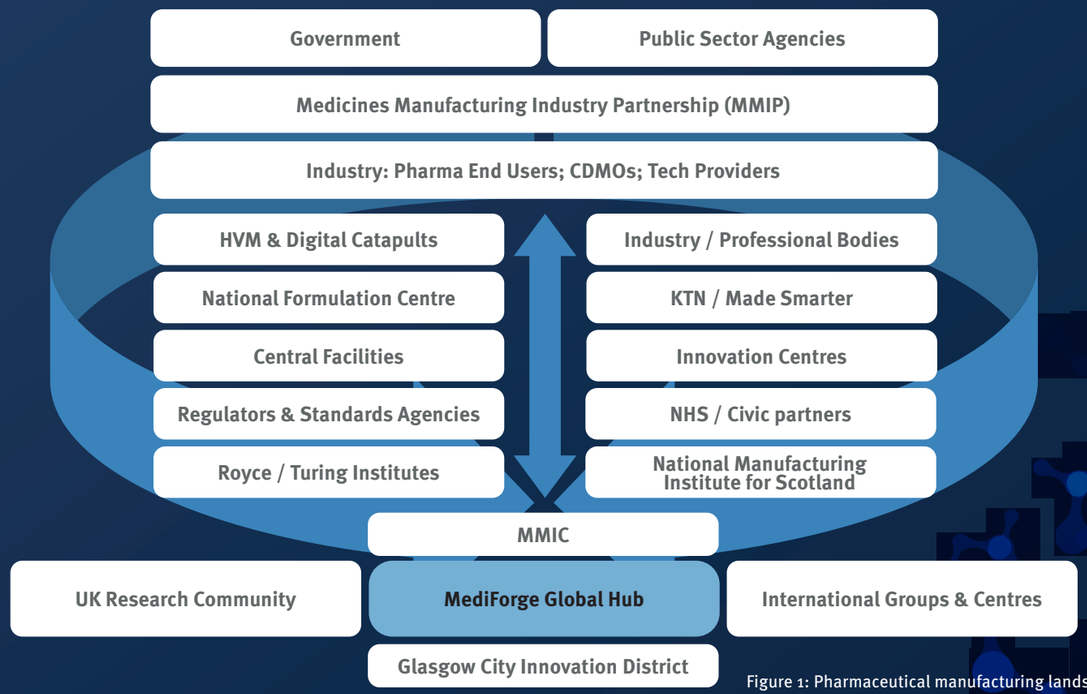


Figure 1: Pharmaceutical manufacturing landscape

Acting as a National Hub

As an EPSRC Manufacturing for Sustainable Futures Research Hub we have a role to work with, and on behalf of, the wider community and to act as a focus for TRL 2-5 research in the medicines manufacturing landscape. We engage and advocate on behalf of the community to influence policy, facilitate and support workshops, meetings and events on topics within our scope. The Hub holds an important position in the collaborative research, development and innovation landscape in the UK.

CMAC is building on over 14 years experience as a pre-competitive, collaborative R&D centre to continue to deliver our Manufacturing the Future research portfolio and training initiatives for medicines development, manufacturing and translation.

NATIONAL HUB ACTIVITIES

- Policy
- Esteem
- Events
- Collaboration and Engagement
- International Network
- Portfolio of Projects Across TRLs

Influencing the Advanced Manufacturing and Digital Ecosystem

AN INTERNATIONAL RESEARCH CENTRE, DRIVING COLLABORATION

White Papers

Business Case Insights; Regulator engagement; International (e.g. CMAC-MIT ISCMP 2014-2021)

National Digital Roadmap

Acting as a National centre

Informing strategy

Additional Recommendations

Engaging stakeholders e.g. data science, digital manufacturing standards, robotics & automation

Influencing Policy

MMIP Skills

Medicines Manufacturing Challenge Community

Manufacturing the Future utilising UK's large facilities

National Skills Agenda

166 PhD students to date

54 Industry placements since 2017

9 CMAC Alumni currently working at Tier 1s

Ongoing: PDRA development; external CPD

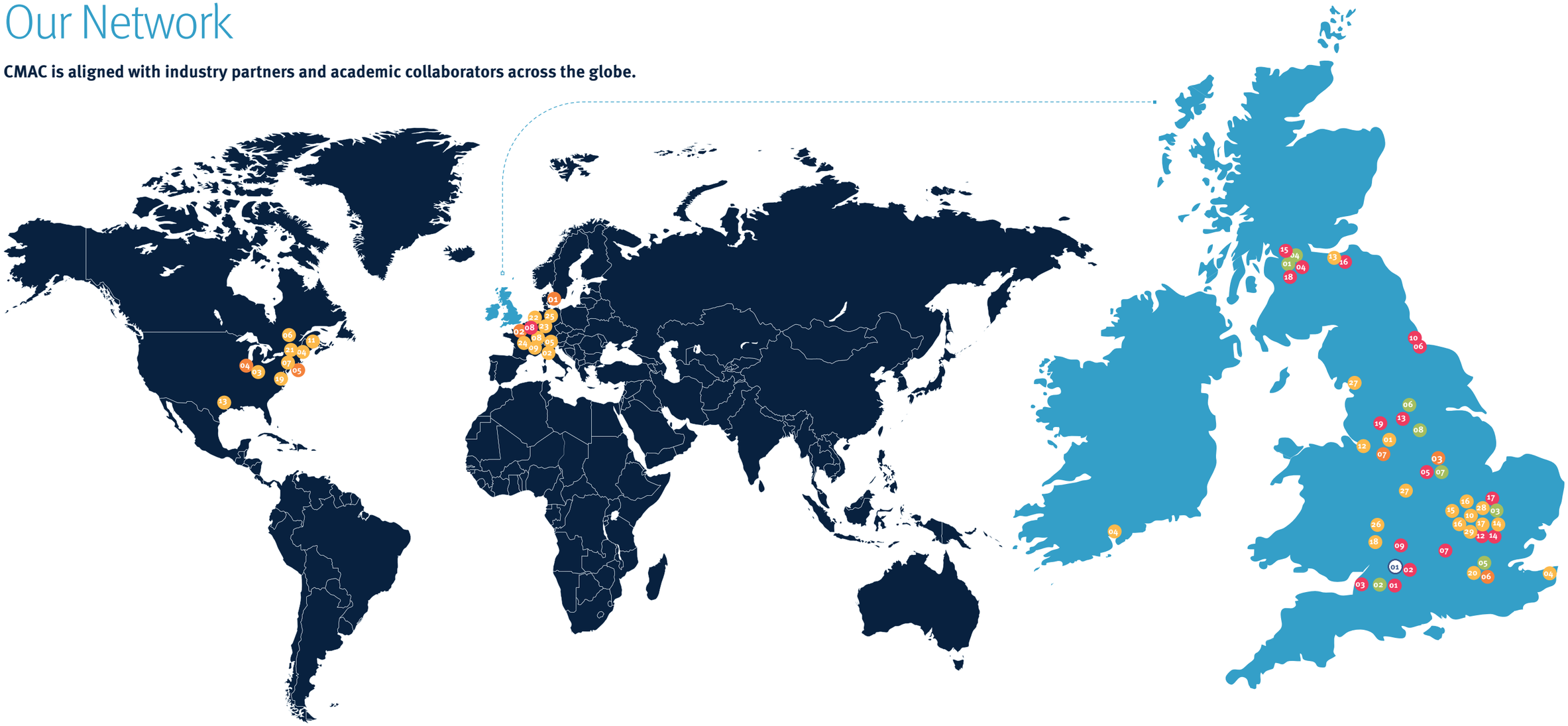
"The demand for multi-disciplinary talent is uniquely served by CMAC"

CMAC INDUSTRY BOARD

- Creating impact from research and application of data and digital technologies
- Input and influence of policy through shaping of roadmaps for digital design, robotics & automation
- Shaping the Skills agenda for the workforce of tomorrow
- Creating infrastructure for the 'Lab of the Future'

Our Network

CMAC is aligned with industry partners and academic collaborators across the globe.



EPSRC:

- 01 EPSRC, Swindon, UK

ACADEMIC HUB AND SPOKES:

- 01 University of Strathclyde, Glasgow, UK
- 02 University of Bath, UK
- 03 University of Cambridge, UK
- 04 Glasgow School of Art, UK
- 05 Imperial College London, UK
- 06 University of Leeds, UK
- 07 Loughborough University, UK
- 08 University of Sheffield, UK

ACADEMIC PARTNERS:

- 01 University of Copenhagen, Denmark
- 02 Ghent University, Belgium
- 03 University of Nottingham, UK
- 04 Purdue University, Lafayette, IN, USA
- 05 MIT, Cambridge, MA, USA
- 06 UCL, UK
- 07 University of Manchester, UK

INDUSTRY PARTNERS:

- 01 AstraZeneca, Macclesfield, UK
- 02 Chiesi, Parma, Italy
- 03 Eli Lilly, Indianapolis, USA
- 04 Pfizer, Sandwich, UK, Cork, Ireland & Groton, USA
- 05 Roche, Basel, Switzerland
- 06 Sanofi, Boston, US
- 07 Takeda, Boston, USA
- 08 UCB, Brussels, Belgium
- 09 Ajinomoto BioPharma Sevices, Ghent, Belgium
- 10 CCDC, Cambridge, UK
- 11 DigiM Solution, Boston, US
- 10 CCDC, Cambridge, UK
- 12 Applied Materials, Cheshire, UK
- 13 Altair, Edinburgh, UK
- 14 Analytik Laminar UK (Analytik) Korea (Laminar)
- 15 Clairet Scientific Limited, Northampton, UK
- 16 Element Syft, Cambridge, UK (Element), Christchurch, New Zealand (Syft)
- 17 Huxley Bertram, Cambridge
- 18 Malvern Panalytical, Worcestershire, UK
- 19 M-Star Simulations, Maryland, USA
- 20 Siemens Process Systems Enterprise, London, UK
- 21 Snapdragon Chemistry, Waltham, USA
- 22 Technobis Crystallization Systems, Alkmaar, The Netherlands
- 23 Nvidia, Munich, Germany
- 24 Medelpharm, Beynost, France
- 25 Fette Pharma AG, Köln, Germany
- 26 Kuka, Wednesbury, UK
- 27 Dec Group, Lancashire, UK
- 28 GSK, Stevenage, UK
- 29 Smith & Nephew, Watford, UK

THIRD SECTOR:

- 01 UKRI, UK Research and Innovation. Swindon, UK
- 02 EPSRC, Swindon, UK
- 03 Research England, Bristol, UK
- 04 CRUK, Formulation Unit, University of Strathclyde, Glasgow
- 05 Connected Everything II, Nottingham, UK
- 06 CPI, Middlesbrough UK, Redcar, UK
- 07 Diamond Light Source, Didcot, UK
- 08 ICE Cubes Services, Brussels, Belgium
- 09 Institute of Chemical and Engineering Sciences, Rugby, UK UK
- 10 Materials Chemistry, CPI, Redcar, UK
- 11 MHRA, London, UK
- 12 MMIP, London, UK
- 13 Calderdale and Huddersfield NHS Foundation Trust, Huddersfield, UK
- 14 NPL, Teddington, UK
- 15 Scottish Enterprise, Glasgow, UK
- 16 Scottish Funding Council, Edinburgh, UK
- 17 The Wolfson Foundation, London, UK
- 18 TÜV SÜD, Glasgow, UK
- 19 Henry Royce Institute, Manchester, UK

Policy

- CERSI project has kicked off in late 2024 see page 59
- QbDD Strategy paper will be published in 2025 see page 28-29

VISITORS

During 2024, CMAC has welcomed visits from government, industry and supporting organisations.

In March, CMAC hosted Joe Edwards, Director of UK Competitiveness and Devolved Nations, and Alison Culpan, Scotland Director, from The Association of the British Pharmaceutical Industry (ABPI). This visit facilitated strategic discussions on how CMAC can collaborate more closely with ABPI to support UK national initiatives in medicine manufacturing.

During the summer CMAC welcomed Charlotte Deane, Executive Chair of EPSRC, accompanied by Deputy Executive Chair Jonathan Dawes, Executive Director Partnerships Andrew Bourne, and Head of Executive Chair's Office Neil Robinson. This visit provided an opportunity to showcase the significant progress being made at CMAC.

In late 2024 CMAC was visited by Anas Sarwar from the Scottish Labour Party as part of a wider University of Strathclyde visit.

MSP Kenneth Gibson paid a visit to the centre, gaining an overview of our latest research and a tour of CMAC's laboratory facilities. This visit followed a series of MSP engagements subsequent to CMAC's recent participation in a Cross-Party Group meeting at the Scottish Parliament. The visit provided a platform to discuss strategies for enhancing CMAC's research impact and exploring strategic, long-term funding opportunities. It also underscored CMAC's pivotal role in the broader medicines manufacturing research and innovation landscape, highlighting our contributions across research, training, and industry translation.

INDUSTRY:

- Pfizer senior delegation
- Shimadzu
- Sanofi
- Croda
- Lilly
- AstraZeneca
- Chiesi

Esteem

CMAC PhD Researcher Suruthi Gnanenthiran (Sheffield) was awarded the prestigious Young Chemist Award, sponsored by Scientific Update Ltd. As part of this recognition, Suruthi attended the 10th Winter Process Chemistry Conference in December 2024 and presented her research in a flash presentation and poster.

Images: High profile visitors to CMAC National Facility in 2024

Events

CMAC Hub Showcase

In September 2024, CMAC hosted a Hub Showcase event to disseminate research outputs from the CMAC Future Manufacturing Research Hub - see pages 22-41. Welcoming over 100 people, including a delegation from MMIP, the group took part in lab tours and met with researchers to hear about the latest research innovations.

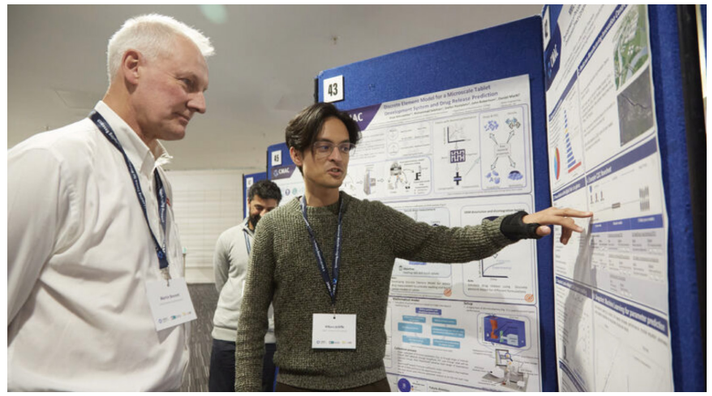


Image: Hub Showcase in September 2024

Image: Creatvity@home training

CMAC Hub Creativity@home

CMAC Hub hosted Creativity@home training for the researchers who were due to transition from old to new projects during 2024. This was a face-to-face event: Impactful Horizons – Navigating your Research Career with Confidence, held in Glasgow and online training modules on grant writing, talks, storytelling and collaboration.

External Events

In March 2024, CMAC researchers attended the 14th World Meeting on Pharmaceutics, Biopharmaceutics, and Pharmaceutical Technology in Vienna, including a presentation by Mohammad Salehian from DM²'s Platform 2 and some posters.

In July 2024, The DM² team attended the Enginuity Skills Awards 2024, and exhibited the Digital Twin of CMAC-DM², an automated microscale manufacturing and testing system, using Augmented Reality.

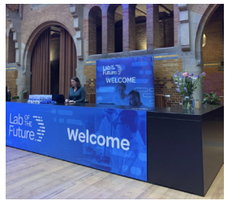
In Summer 2024, The CMAC team attended this year's Compaction Simulation Forum in Dublin, featuring a presentation from Professor Daniel Markl, as well as poster presentations from CMAC researchers.

CMAC's Senior Project Scientist Carlota Mendez Torrecillas presented at Formulation 4.0 event hosted by RSC Formulation Science & Technology Interest Group and Physical Analysis Technician, Rachel Feeney, was delighted to attend and speak at the Blue Scientific Ltd. CT and SEM open day at Alderley Park - both in summer 2024.

Hannah Batchelor presented at the International Scientific Association for Probiotics and Prebiotics (ISAPP) 2024 Annual Meeting. CMAC sponsored PharmTech Integrates 2024 and hosted tours of its National Facility.

CMAC had a presence at Pharmatech Integrates 2024 and were a sponsor of the event and hosted lab Tours of the CMAC National Facility.

Also in autumn 2024, CMAC participated in Lab of the Future in Amsterdam, the Scottish Graduate Fair in Glasgow, the 29th BIWIC International Workshop on Industrial Crystallisation at Delft University of Technology in the Netherlands, Pharmaceutical Solid State Research Cluster (PSSRC) Symposium in TU Dortmund, Germany, SciX 2024, Scotland Manufacturing and Supply Chain, CAMS Conference and Networking Event, European SIFT-MS Symposium, APS PharmSci, 34th European Crystallographic Meeting, and AIChE 2024.



Images: CMAC team at events in 2024

Collaboration and Engagement

INDUSTRY PARTNERS

New Partners in 2024

Sanofi, a leading global pharmaceutical company, joined CMAC as Tier 1 Partner in February 2024. Sanofi's expertise will further strengthen CMAC's research portfolio. Their dedication to Digital Transformation of CMC (Chemistry, Manufacturing and Control) seamlessly aligns with CMAC's vision to revolutionise medicines manufacturing, fostering a sustainable and impactful approach.

In February 2024 CMAC welcomed Malvern Panalytical as a new Tier 2 member. Already a key stakeholder in our Digital Medicines Manufacturing research centre (DM2), Malvern Panalytical will be further embedded within our digital Manufacturing Classification System (MCS+) research strategy to collaboratively drive progress in CMAC DataFactories and advanced application of analytical data.

In September, global CDMO Ajinomoto Bio-Pharma Services became the first Translation to Industry Collaborator within CMAC. As a CDMO, Ajinomoto will play a significant role in the pharmaceutical industry with its ambition to enhance expertise in crystallisation, Process Analytical Technology (PAT), continuous manufacturing, and digitisation.

Also in September 2024 digiM Solution joined CMAC as a Tier 2 member. CMAC will utilise the digiM Image 2 Simulation (I2S) software to enable the analysis of imaging data collected within its world-class facilities. Support will include work towards the cutting-edge research in CMAC's DataFactory programme and will accelerate advanced understanding of drug product manufacturing, performance, and stability through quantitative analysis of cutting-edge X-ray computed tomography and other image-based data.

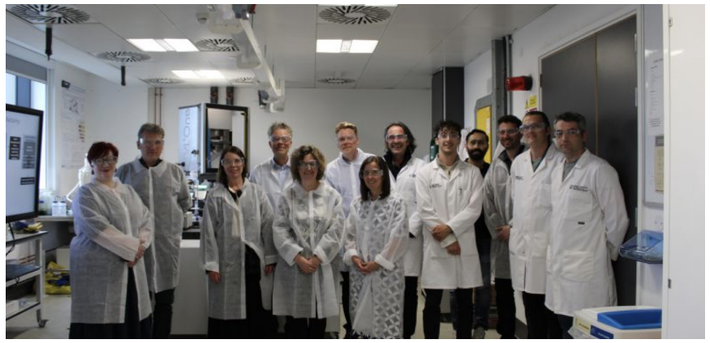


Image: Visit by AZ

Industry Partner Engagement

Tier 1 partners, AstraZeneca, visited CMAC in Glasgow in summer 2024. The visit further enhanced our collaborative engagement and aligned our strategies going forward, building upon input and direction for future programmes, including the CEDAR CDT. CMAC researchers and staff had the opportunity to discuss and demonstrate their research and outputs across drug substance, drug product, and digital platforms, highlighting their significance for industrial application.

CMAC appointed John Mack, Head of Perceptive Advanced Process Control at Applied Materials, as a new member of its Industry Board in early 2025. Representing CMAC's Tier 2 membership, John's role will enhance the Tier 2 community's connection to CMAC's activities, ensuring the centre stays at the forefront of manufacturing advancements and continues to meet the evolving needs of its members.

CMAC Data Lab team visited NVIDIA's Executive Briefing Centre in Munich at end of 2024. During the visit, the team engaged in thought-provoking discussions and explored the latest advancements in AI and machine learning to optimise the impact of recent investments in GPU and edge computing, directly benefiting CMAC's research and training programmes.

Image: Prof Alastair Florence and John Mack

Image: RiFTMap Technical Meeting in Glasgow 2024

ACADEMIC ENGAGEMENT

International

CMAC was thrilled to host the technical meeting for the pioneering 'Right First Time Manufacture of Pharmaceuticals' (RiFTMaP) programme here in Glasgow in 2024. The meeting brought partners together, providing a dynamic platform for updates on each work package, insightful discussions on future developments and fostering collaboration from an industrial perspective. This ambitious programme, funded by the EPSRC and the US National Science Foundation (NSF), is led by the The University of Sheffield, with academic partners including the University of Strathclyde, UCL and Purdue University (USA). This is supported by an array of industrial partners from the pharmaceutical, software, and equipment manufacturing sectors. See also page 53 for more about the research.

CMAC's Directors Alastair and Massimo visited Singapore in the summer. They visited the Advanced Remanufacturing and Technology Centre (ARTC), leadership and academic teams from the Singapore Institute of Technology and the National University of Singapore to explore the transformative potential of research and innovation in pharmaceutical manufacturing, focusing on cutting-edge, pre-competitive research.

UK

CMAC recently welcomed Prof George Panoutsos and Dr Kai Eivind Wu from the University of Sheffield for discussions on their completed CMAC Hub feasibility project and potential future collaborations. During their visit George and Kai delivered an outstanding seminar on Many Objective Optimisation Modelling. The seminar focused on the results of two case studies using data supplied by CMAC. The visit offered an excellent opportunity to explore how Many Objective Optimisation Modelling can drive advancements in CMAC's research.

Image: Seminar by Prof George Panoutsos and Dr Kai Evind Wu

Public Engagement

Throughout 2024, the Digital Manufacturing Research Centre (DM²) team engaged with public groups from across the Renfrewshire region. Recognising the important role in building trust in the use of data and industrial digital technologies in medicines manufacturing, the team engaged with U3a, a UK-wide network.Initial engagements took place with two branches of U3a: Newton Mearns in East Renfrewshire in March 2024, and Bearsden in East Dunbartonshire in August 2024. The team met with around 30 attendees at each session, which included an informative presentation by our DM² representatives and a Q&A. Learnings from the U3a participants were gathered and fed back to the research team.

Image: U3a Session by DM2 team

To grow our outreach, CMAC made a podcast about CMAC Future Manufacturing Hub research as a SciPod recording, available on Spotify: https://lnkd.in/eBFwkeD5

VISITING RESEARCHERS:

- **Mingrui Ma (Cambridge)**
- **Kensaku Matsunami (Ghent)**
- **Joona Sorjonen (Finland)**

Research Excellence & Intensity

RESEARCH GOALS

Our aim is to enable the digitalisation of Chemistry, Manufacturing and Control (CMC) processes and establish Cyberphysical Systems (CPS) for medicines development and production processes through our platform technology areas. This will be achieved through the development of the following framework of integrated solutions:

- A Quality by Digital Design (QbDD) Framework that integrates multiple workflows and technologies to achieve digital design of primary particles, products and their associated manufacturing processes and supply quickly, robustly and sustainably
- Three novel predictive Classification Systems (see below) spanning the production of primary particles to formulated product and addressing manufacturability, stability and performance:
  - CCS: accelerate development of particles (Crystallisation Classification System, CCS),
  - MCS+: inform the selection of manufacturing route (Manufacturing Classification System+, MCS+)
  - BPCS: and aid in the design of optimally performing medicines (Biorelevant Performance Classification System, BPCS)

MOLECULE › PARTICLE › BULK › PRODUCT & PROCESS › PERFORMANCE › QUALITY TO PATIENT

Research Platform	Crystallisation Classification System (CCS)	Manufacturing Classification System+ (MCS+)	Biorelevant Performance Classification System (BPCS)	Quality by Digital Design (QbDD) Methods
Purpose	Develop integrated platform/s to support efficient and science driven development from molecule to particle	Assess manufacturability suitability across drug substance and drug product focusing on specific yet critical unit operations	(i) Identify effective range of release achievable in population subsets (ii) develop new release systems that self learn from clinical outcomes and/or endpoints	Exploit digital design workflow to model, understand and optimise design space
Scope	• Exploit physics-based, data-driven AI/ML and hybrid models to inform process selection and design • Suggest experiments to perform into improve predictions and understanding • Implement molecule and particle risk assessment of crystallisation outcomes"	• Exploit process Digital Twins, material property databases and predictive tools for key operations • Build on MCS for drug product • Implement particle and bulk property assessment to predict outcomes	• Build on Biopharmaceutical & Developability Classification Systems • Connect to PBPK & population based PK models • Integrated with AI self learning • In silico population bioavailability distribution • Suggest experiments to perform into improve predictions and understanding	• Model driven identification of CMAs, CPPs & CQAs • Product and process understanding • Global sensitivity for integrated processes • Develop and translate commercial digital solutions ready for industrial application & NDA submission
Refer to pages for more details	• Pages 30-31 for CCS and CSDF	• Pages 34-35 for Hub MicroFactories • Pages 54-55 for DM2 • Pages 60-61 for MMIC GC1	• Page 50 (GIBio)	• Pages 28-29 for QbDD

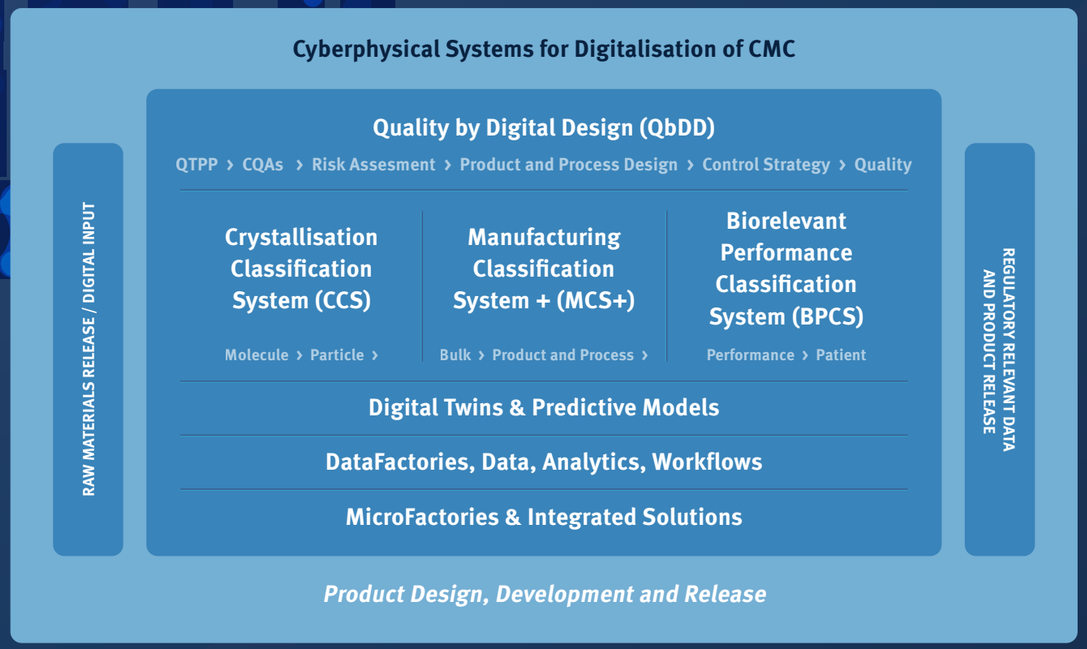


Figure 2: 2021+ Research Direction: Building integrated solutions to transform development and manufacture of medicines, combining the academic expertise across our platforms and enabling capabilities to deliver an integrated platform for QbDD as a framework for digitalisation of CMC.

CMAC DataFactory - Autonomous AI and collaborative robotics enabled development platforms

Overview of CMAC Research Programme

CMAC has a dedicated team of ~140 colleagues delivering a research and translation programme that is addressing challenges and sourcing solutions to build a more human-centric resilient and sustainable supply chain for medicines manufacturing.

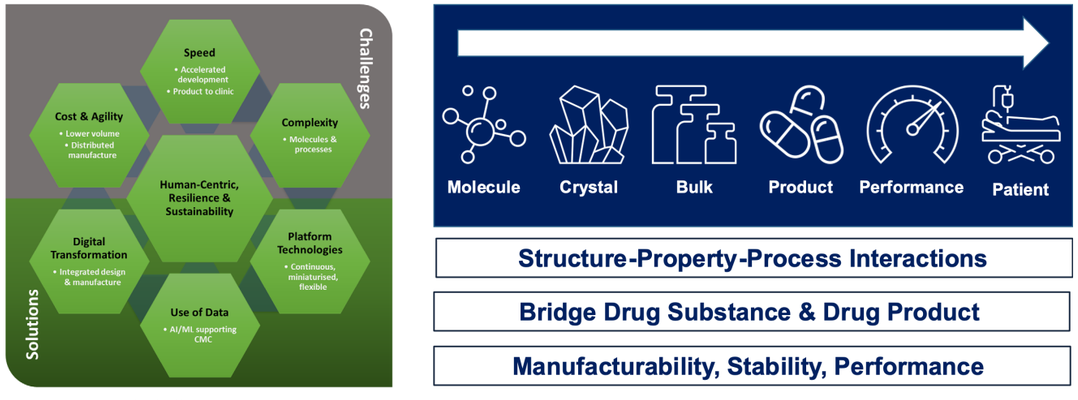


Figure 3: Research challenges

In 2023-24, CMAC launched three new research projects with funding from UK government. Each programme is aligned to the CMAC pillars (page 6).

Research Excellence & Intensity	Outstanding Skills Development	World Class Facilities	Exemplary Translation to Industry
MediForge Industry 5.0 Medicines Manufacturing Research Hub	CEDARCDT EPSRC Centre for Doctoral Training in Cyber-Physical Systems for Medicines Development and Manufacturing	CMAC DATALAB A Digital Medicines Manufacturing Research Accelerator	CMAC
EPSRC Manufacturing Research Hub for Sustainable Future	EPSRC Centre for Doctoral Training	UK RPIF Capital Award	Translation to Industry (T2I)
Award: £11M, 2024-2031	Award: £10M, 2024-2032	Award: £11M, 2023	Multiple Funding Routes
Strathclyde, Leeds, Sheffield, Imperial & Glasgow School of Art	Strathclyde, Leeds, Sheffield, Imperial	Strathclyde – critical mass; access to all partners	Core Projects; National Facility Innovate UK e.g. DDAP; Made Smarter
Team of 10 PDRAs	Train 90 PhDs over 5 intakes	Builds on two previous awards to ensure state-of-art facilities for research, training and T2I	Knowledge Transfer Partnerships (KTP)
Develop end-to-end cyberphysical infrastructure	Develop cyberphysical systems	Enable purchase of cyberphysical components: process platforms;PAT; robotics; CPU/GPU; data fabric (KG); visualisaton; characterisation	Impact Acceleration Account (IAA) £5M Place Based Impact Acceleration Account (PBIAA) Underway
Embed sustainability objective	Operating in Research Challenge Teams		

Figure 4: Projects aligned to 4 Pillars

Research Portfolio

CMAC'S RESEARCH PORTFOLIO IS DRIVEN BY A CORE ACADEMIC TEAM WITH THE UNDERPINNING RESEARCH EXPERTISE AND CAPABILITIES TO DEVELOP NEW INTEGRATED SOLUTIONS ACROSS OUR MEDICINES MANUFACTURING SCOPE.

CMAC's strategy builds on the CMAC Hub project and is informed by the project portfolio of industry demand led manufacturing research. Academic strengths cover a breadth of areas and are focussed on developing capabilities in:

- Next Generation Solid State
- Smart Crystallisation, Particle Engineering and Isolation
- Smart Formulation and Drug Product Processing
- Biorelevant Release and Real-time Release Testing
- Advanced Characterisation
- Next Generation Digital
- MicroFactories

In growing the critical mass of projects and facilities around the Hub platform, our goal is to work collaboratively to identify priority areas where we can develop further activities that target additional manufacturing research and address key industry areas of need.

Cross-cutting Topics	TRL	Crystallisation & Isolation	Particle Engineering	Advanced Drug Product Development	Biorelevent Performance Design	
Data & DataFactories - smart development platforms; Digital Twins - modelling and prediction; Workflows - model driven experimental design; MicroFactories - modular, flexible processing; Net Zero - sustainable development & processes	TRL 7-9	Potential industry demonstrators, spin-outs, in-house company projects				Deploy
	TRL 4-6		CAMS			Validate
				MMIC GC1		
		CMAC National Facility Projects				
		CERSI EOI/ Full				
		DPN-MED EOI				
		KTPs				
		SHARPEN				
		CMAC Core & Propietary Projects				
		Made Smarter Innovation - Digital Medicines Manufacturing (DM2) Research Centre				
	TRL 1-3	EPSRC MediForge Hub (started Oct 2024)				Understand
		EPSRC Future Continuous Manufacturing & Advanced Crystallisation Hub (ended Sept 2024)				
		RiFTMaP				
			3DP			
		EPSRC Prosperity Partnership				
		SolvIT				
		EPSRC Digital Design and Manufacture of Amorphous Pharmaceticals (DDMAP)				
		PharmaCrystNet				
		CEDAR CDT				
		CMAC PhD Portfolio				
		RPIF - DataLab				Discover
		RPIF - NetZero				
					EPSRC Strategic equipment (GIBio)	
Embedded: Training & Skills; Advanced Technology & Facilities; Translation to Industry						

Future Continuous Manufacturing and Advanced Crystallisation Research Hub

EP/P006965/1 - FINAL REPORT - JAN 2017-SEPT 2024

270 PUBLICATIONS	166 TALKS	124 POSTERS	22 PHD THESES
5 OPEN DAYS	40% PDRA NEXT DESTINATION IN INDUSTRY, 54% IN ACADEMIA	39 FURTHER FUNDING PROJECTS (INCLUDING PHD PROJECTS)	CMAC ALUMNI WORKING AT TIER 1 COMPANIES
SAVED COMPANIES >£20M P.A.	12 CMAC ALUMNI WORKING AT TIER 1 COMPANIES	£25M CRITICAL MASS FUNDING FROM EPSRC	43 FUNDED PROJECTS

OVERVIEW

The Future Continuous Manufacturing and Advanced Crystallisation Research Hub (EP/P006965/1) - known as the Hub - was a collaboration between University of Strathclyde and spokes University of Bath, University of Cambridge, Imperial College London, University of Leeds, Loughborough University, and University of Sheffield.

It was supported by EPSRC and CMAC Tier 1 industry partners and Tier 2 Technology companies. Hub research underpinned the CMAC research portfolio during that time and the Hub acted as a National Centre for the medicines manufacturing research community with focus on TRL 2-5 research

THIRD SECTOR PARTNERS

EPSRC CMAC Future Manufacturing Research Hub Programme

The Hub was a flagship programme as part of EPSRC critical mass investments in future manufacturing research.

HUB VISION

Revolutionise the development and supply of functional, high-value chemical and pharmaceutical products by delivering a rapid, digitally-enabled pipeline to integrated continuous manufacturing processes.

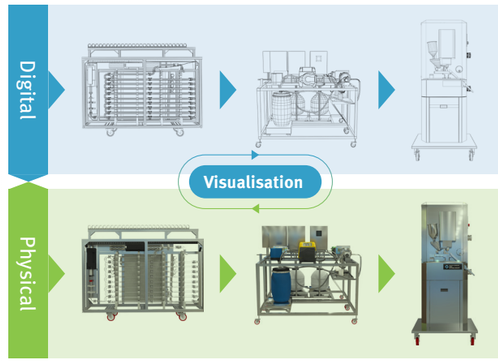
PROGRAMME VISION

Key goals:

- Minimal material and experiments via predictive modelling
- Crystal attributes for enhanced manufacturability, stability and performance
- Integrated, flexible continuous process streams

Example process:

crystallise ▸ isolate ▸ compress ▸ test



1: Small Scale Experiments & Predictive Tools

Measured and predictive parameters

2: Dynamic Process Models

Predicted process performance and product attributes

3: Operate Using Flexible, Integrated Platforms

Reduced materials, cost & time plus enhanced quality

QbDD Workflow – library of workflows to set objectives and drive team from digital design to manufacture

DataFactories – access to experimental data to drive model building, development, testing and validation

Digital Twin – Model and Data libraries across materials, equipment, processes and products

MicroFactory – Modular, flexible continuous processing test beds of API and DP – validate models, control of material attributes

Establish digital design and digital manufacturing concepts for modular, integrated continuous processes

Figure 5: Hub Programme

HUB GOALS

- Develop products and processes using minimal material and experiments exploiting predictive modelling and data
- Understand and control crystal and material attributes for enhanced manufacturability, stability and tailored performance
- Demonstrate modular, integrated, flexible multi-product and/or tailored product specification MicroFactories to enable future supply chains

Image: Dosing solids in the Crystallisation DataFactory

Acting as a National Hub

The CMAC EPSRC Future Manufacturing Research Hub had a role to work with, and on behalf of, the wider community and to act as a focus for TRL 2-5 research in the medicines manufacturing landscape. We engaged and advocated on behalf of the community to influence policy, facilitate and support workshops, meetings and events on topics within our scope.

POLICY

The Hub had a role to act as a National Hub throughout the project and as such has aligned with key policy.

Policy work has included alignment with the MMIP mission to support the UK to become a leading force in manufacturing innovation, ABPI's Manufacturing vison for the UK, The Made Smarter Report, FDA vision for Global Pharma, National Digital Roadmap and National Skills Agenda during the period 2017-2024.

In 2021 CMAC reached its 10-year anniversary and published CMAC Strategy 2021-2026 (https://cmac.ac.uk/cmac-business-case-strategy The strategy includes aiming to achieve greater speed, quality, agility, security and sustainability, in pharmaceutical manufacturing and communicating and engaging around the need for advanced pharmaceutical manufacturing, analytics and industrial digital technology development.

The outputs of the Hub include a perspectives paper on QbDD strategy (submitted to IJPX), and contributions to white papers on Business Case Insights and Regulator engagement.

Recently, CMAC made a presentation to Scottish Life Sciences Cross Party Working Group and Finance and Administration Committees, highlighting the high return on investment demonstrated from manufacturing research investment and advocating for further investment in medicines manufacturing research.

The work in development of digital tools and autonomous lab systems for medicines development has also informed our successful CERSI bid, that will deliver pathway to impact with UK (MHRA) and international regulators (e.g. FDA) for the standardisation of assessment and evaluation frameworks for digital tools in CMC submissions.

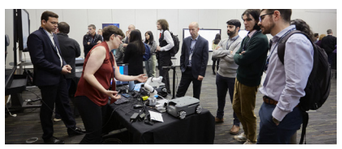
The need for skilled people to address the gap in Digital Transformation and Data-Driven Research has been highlighted in the policy work done by the Hub. The CMAC Skills pillar starts to address the requirements of the talent pipeline, and our industry partners have noted how the doctoral training at CMAC produces uniquely skilled people. Significant further funding towards training has been awarded because of the Hub award, including the CEDAR Centre for Doctoral Training award that started in 2024.

ESTEEM

The University of Strathclyde received Queen's Anniversary Prize for Higher and Further Education in 2023. The award, which is the highest national honour in the sector, was conferred on University of Strathclyde for its excellence in Advanced Manufacturing with CMAC a key contributor to that award.

Other high impact achievements included CMAC featuring in UK manufacturing outlook 2022, a REF21 impact case study published in 2022.

Image: Prof Florence receives the Queen's Anniversary Prize in 2023



Images: CMAC Open Days

ENGAGEMENT

Public Outreach

The CMAC Hub has online presence (CMAC website, YouTube, LinkedIn) and has engaged annually in face-to-face public outreach activities to share the benefits of the work done in the Hub.

Events

CMAC hosted five Open Days Events over the period of the CMAC Hub award, with the CMAC Hub being the main sponsor and organiser of the event. The main audience was the CMAC network and the event was open to anyone interested in finding out more about the CMAC Hub

The Open Days have been established as a way for industry and the third sector to engage with CMAC and find out about the recent research outputs from the portfolio of projects and current capability available.

Hub Director Prof Alastair Florence has been on the Organising Committee for the biannual ISCMP/ICAMM events for the duration of this award. It is an event that influences regulators and high-level decision makers in the sector

In September 2024 a one-day Showcase event was hosted in Glasgow to disseminate the Hub outputs. The main audience included a senior delegation from MMIP who toured the labs in TIC, University of Strathclyde and saw talks and a poster session with highlights from the programme. This event helped to raise awareness of the strong alignment and contribution CMAC was making through research programmes in advanced medicines manufacturing, digital transformation and sustainability initiatives. This has led to further discussions with ABPI on how best to ensure benefit from CMAC programmes can be achieved across the UK ecosystem.

Moving forward CMAC will continue to host and organise internationally important events for the Pharmaceutical Manufacturing Community.

Industry Engagement

CMAC industry members over the duration of the project included:

Tier 1

AstraZeneca, Bayer, Chiesi, GSK, Lilly, Novartis, Pfizer, Roche, Sanofi, Takeda, UCB

Tier 2

Applied Materials, Altair, Anatune, Analytik, AWL, Blacktrace, Booth Welsh, Buchi, CCDC, Clairet Scientific Ltd., Dec Group, digiM, EDEM, Element Syft, Fette, Huxley Bertram, Kuka, Malvern, Medelpharm, Mettler Toledo, M-Star, Nitech, Nvidia, Pion, PwC, QbD Vision Cherrycircle, Siemens PSE, Snapdragon, Sirius Analytical, Technobis, ThermoFisher Scientific.

Many of these continue to support CMAC beyond the end of this award. It is notable that we have attracted new partners (e.g. Sanofi, Lonza, Ajinomoto) during this period illustrating the international profile the centre has developed.

Other Supporters

Other Hub supporting organisations included: ADDoPT, Cancer Research UK, Connected Everything, CPI, Diamond, IceCubes, KTN, Materials Chemistry, MHRA, MMIP, NTU, NPL, RCPE, ReMediES, Scottish Enterprise, and Scottish Government.

Academic Engagement

The Hub has engaged with other academic and industry groups via feasibility studies, engaging a group of visiting professors and regularly hosting workshops and seminars throughout the project.

INTERNATIONAL NETWORK

During the Hub award period, CMAC's portfolio of projects included the international collaborative projects I2APM (EP/M021661/1),DDMAP(EP/W003295/1), and RiFTMaP (EP/V034723/1) as well as the contribution to organising the biannual ICAMM/ISCMP events noted above.

PORTFOLIO OF RESEARCH PROJECTS

The UK has supported the portfolio of aligned projects underpinned by the Hub investment. CMAC's strategy 2021-2026 built on the CMAC Hub and aligned project portfolio and was informed by the project portfolio of industry demand led manufacturing research. In growing the critical mass of projects and facilities around the Hub platform, we achieved our goal of working collaboratively to identify priority areas where we can develop further activities that target additional manufacturing research and address key industry areas of need. This resulted in over 43 further funded projects with a value of ›£56M.

SKILLS

The need for skilled people to address the gap in Digital Transformation and Data-Driven Research has been highlighted. The UK has supported the portfolio of aligned projects underpinned by the Hub investment. The CMAC Skills pillar starts to address the requirements of the talent pipeline, and our industry partners have noted how the doctoral training at CMAC produces uniquely skilled people. Significant further funding has been awarded because of the Hub award, including the CEDAR Centre for Doctoral Training award that started in 2024.

Hub Research 2017-2024

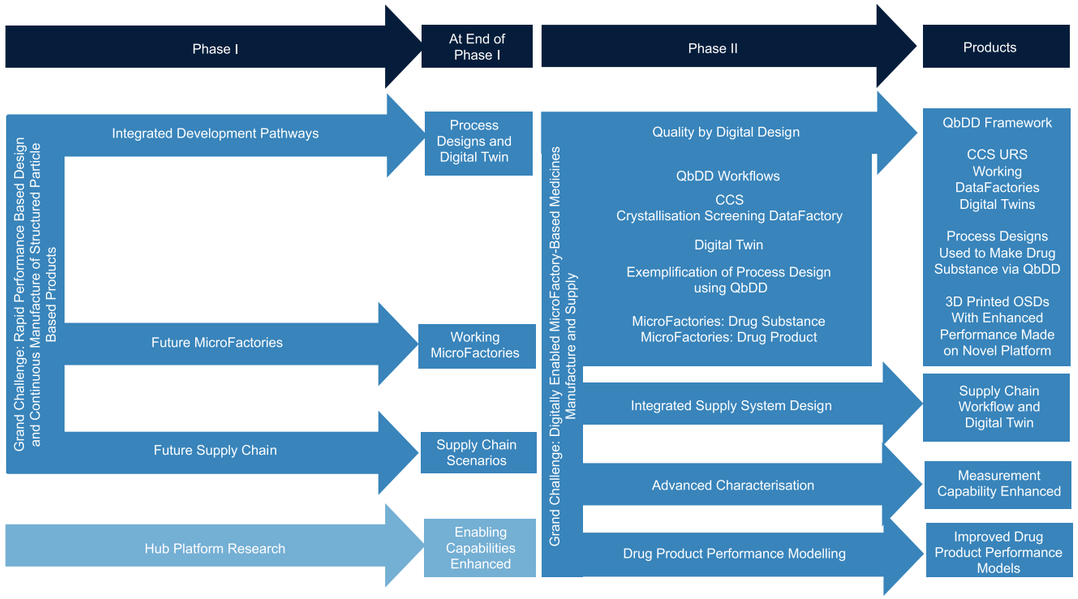


Figure 6: Overview of Phase I & II activities and products for the CMAC Future Manufacturing Research Hub programme – Jan 2017 to Sep 2024.

IMPACT FROM THIS PROGRAMME INCLUDES:

- Accelerated development of product and optimised manufacturing processes
- Closer integration of Drug Substance and Drug Product manufacture
- Increased use of Digital Twins to drive MicroFactory design, operation and control
- Advanced characterisation capability advanced across length scales from the molecule to the particle
- Enhanced of Drug Product Performance model capability

Image: Lab of the Future

SUMMARY OF RESEARCH OUTPUTS

Quality by Digital Design

Quality by Digital Design (QbDD) advances the FDA's Quality by Design (QbD) by integrating modelling and digital tools to drive sustainable, efficient, and innovative pharmaceutical manufacturing. Applied to three API processes, QbDD delivered up to 65% material savings and reduced experiments by 28% through digital optimisation. Our 2023 study showcased a digital-first approach to designing mefenamic acid production, enhancing process robustness, flexibility, and speeding up medicine development.

More information: See pages 28-29, Transforming Pharmaceutical Manufacturing with Quality by Digital Design to Accelerate Sustainable Medicines Development - pre-print publication **https://doi.org/10.1016/j.ijpharm.2025.125625** and flyer **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1ebda73d3c378c02b4ff/1745493697352/QbDD+Strategy.pdf**, Transforming Pharmaceutical Manufacturing with Quality by Digital Design - **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1df4bb58e75d29a07ba5/1745493497416/QbDD+Exemplar.pdf**, and Exploiting Digital Tools for Pharmaceutical Quality Attribute And Process Design: **Making Medicines More Sustainably**

Crystallisation Classification System (CCS)

Developed with Tier 1 partners, the CCS URS defines key capabilities of CMAC's predictive digital framework for CMC development. It integrates models, experiments, and workflows to accelerate medicine development. The URS highlights CCS's value, technical deliverables, prediction accuracy, and data needs, guiding current and future research beyond CMAC.

More information: See page 30 and A Crystallisation Classification System to Accelerate Sustainable Medicines Development - **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1b1d45827e07cbbff86a/1745492768993/CCS.pdf**

Crystallisation Screening DataFactory (CSDF)

The CSDF is an autonomous robotic platform for crystallisation process optimisation. Using QbDD and CCS URS guidance, it combines cobots, automated dosing, and machine learning-driven experimentation. Developed in Phase II, it ensures FAIR data collection, with key datasets stored for future use. Expansion continues through the RPIF Round 7 Data Lab award.

More information: See page 31, and A Crystallisation Screening DataFactory to Advance Medicines Manufacture – https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1b82e114373f3e12f10d/1745492870205/Crystallisation+Screening+DataFactory.pdf

Digital Twins Framework

At CMAC, we've developed an integrated Digital Twin framework to accelerate the design, control, and optimisation of continuous drug manufacturing processes. Our platform connects data, models, and knowledge across Drug Substance crystallisation and Drug Product production, powered by our DataFactories and MicroFactories. Our digital toolbox includes predictive models for morphology, solubility, and solvent selection, and our QbDD workflows. Our AssetStore digital library captures and manages assets we have developed, enabling data-driven, efficient process innovation.

More information: See pages 32-33

MicroFactories

Our Drug Substance MicroFactory features a flexible MSMPR system operating in batch or continuous modes, with configurable vessels, residence times, and slurry transfer options. Equipped with advanced filtration, washing, and drying units—including the AWL CFD25 carousel filter—and PAT-enabled real-time control of Critical Quality Attributes (CQAs), the platform has demonstrated QbDD principles across four API processes.

CMAC developed a filament-free 3D printer (UK patent application 2101534.2) for pharmaceutical additive manufacturing. It successfully printed a previously unprintable Soluplus®-based formulation, achieving targeted immediate release dissolution profiles, demonstrating its potential to streamline pharmaceutical processing.

More information: See pages 34-35 and Expanding the Pharmaceutical Formulation Space in Material Extrusion 3D Printing Applications – **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/68147faa3d81f83f7d21589e/1746173871966/Secondary+Processing+%281%29.pdf**

Advanced Characterisation

CMAC's Advanced Characterisation research integrates cutting-edge analytics with UK national facilities like Diamond Light Source and the Henry Royce Institute, fostering multi-institution collaboration at Harwell.

More information: See page 38, Particle, Fluid and Impurity Transport During Filtration, Washing and Drying - **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a2053ff14e24e543c4f71/1745494103030/XPCT+Isolation.pdf**, and Understanding of Amorphous Solid Dispersions: An Interplay Between Saturation, Temperature and Structure - **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1c257927892acf405acf/1745493033306/Drug+saturation+processing.pdf**

Spherical Agglomeration

The Hub developed a mechanistic understanding and model-driven workflow for spherical agglomeration, introducing the True Bridging to Solid Ratio (TBSR) to simplify solvent selection. The work also generated a kinetics model for agglomerate formation and a population balance model, providing a structured approach to process design.

More information: See page 36 and Mechanistic Understanding of Spherical Agglomeration Processes – **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1fd38ac57a1aa147baod/1745493976804/Spherical+Agglomeration.pdf**

Drug Product Performance Modelling Capability

Mechanistic models have been developed to describe important rate processes driving OSD dispersion, dissolution and disintegration. Also, novel characterisation techniques such as optical coherence tomography (OCT) have been employed to visualise evolving OSD microstructure over time. The recent work has been focused on model development, experimental validation techniques and the implementation of models into existing and in-development model platforms for OSD manufacture.

More Information: See page 36

Supply Chain

The Hub supply chain research took a multidisciplinary approach to assess how advanced manufacturing technologies can transform pharmaceutical supply networks. Aligned with the QbDD workflow, the team identified and evaluated reconfiguration opportunities using diverse methods. These included molecule and technology selection based on managerial and engineering principles, expert judgment structuring via digital apps and structural modelling and assessment of investment opportunities in advanced manufacturing and digital infrastructure.

More Information: See page 37

Feasibility Studies

The Hub conducted four key feasibility studies that allowed the Hub to engage with the wider community, highlighting orthogonal approaches to long standing challenges and identify potential new collaborations. A number of papers were published from this work and at least one collaborative grant submission generated.

More information: CMAC Hub Feasibility Projects - **https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1d39e37a2e1af15b0546/1745493309147/Feasibility+Studies.pdf**

Key Achievements

Quality by Digital Design

AIM:

- Create a QbDD strategy and framework to drive process development

EXPECTED IMPACT:

- Move industry beyond empirical or 'one-experiment-at-a-time' development approaches
- Accelerate development of product and optimised manufacturing processes
- Closer integration of Drug Substance and Drug Product manufacture

Work on the Hub developed a shared industry-academic perspective on the principles and opportunities for Quality by Digital Design (QbDD) as a framework to accelerate medicines development and enable regulatory innovation for new medicines approvals. This approach exploits emerging capabilities in industrial digital technologies to achieve robust control strategies assuring quality whilst reducing development time/costs, improving research and development efficiency, embedding sustainability into new products and processes, and promoting supply chain resilience.

Key QbDD drivers include the opportunity for new scientific understanding and advanced simulation and model-driven, automated experimental approaches. QbDD explores the complex, multi-factor process and product knowledge space to identify a robust design space. Opportunities to optimise multiple objectives emerge in route selection, manufacturability and sustainability whilst assuring product quality. Challenges to QbDD adoption include siloed data and information sources across development stages, gaps in predictive capabilities, and the current extensive reliance on empirical knowledge and judgement. These challenges can be addressed via QbDD workflows; model-driven experimental design to collect and structure findable, accessible, interoperable and reusable data; and chemistry, manufacturing and control ontologies for shareable and reusable knowledge. Additionally, improved product, process, and performance predictive tools must be developed and exploited to provide a holistic end-to-end development approach.

The Hub work on QbDD created a Framework of process and sub-process workflows for delivery of manufacturing processes. This was exemplified by delivery of a total of four API MicroFactory processes.

In Phase I the Hub team started work on the digital design of a Mefenamic Acid Drug Substance MicroFactory Process. This produced an end-to-end purification, particle engineering and isolation flowsheet, flowsheets for individual continuous crystallisation, isolation and washing implemented in gPROMs and design space for process to make Mefenamic Acid API via continuous process simulation.

From QbD to QbDD

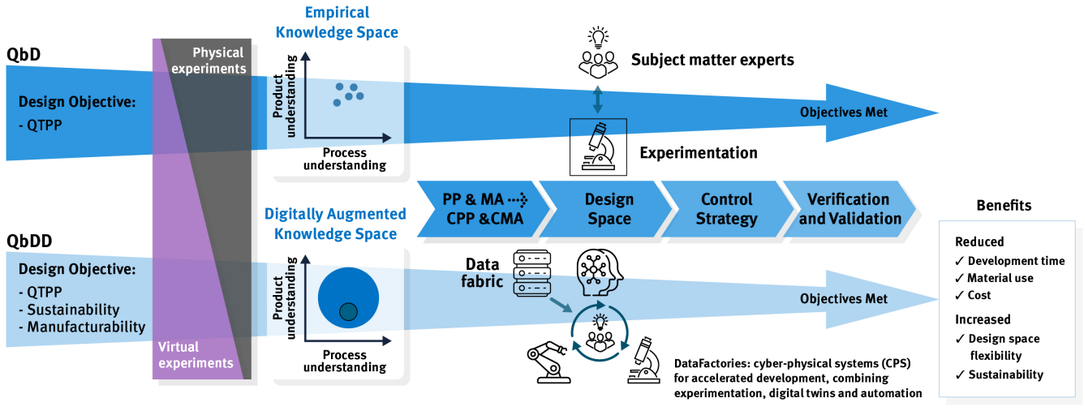


Figure 7: The transition from QbD to QbDD with reference to its effect on the knowledge space

BENEFITS OF DIGITAL-FIRST

- Digital-first will reduce development time, cost, and resource requirements
- Enables the design of robust manufacturing processes, enhancing flexibility in design space operation through "Quality by Digital Design"

In Phase II the Hub continued the work to deliver processes via a digital-first approach and used the learnings to create version 1 of the QbDD workflows. Then the team went on to use the QbDD workflows to deliver three more case studies and refine the QbDD workflow to version 2. There are two papers about the Drug Substance process design using QbDD: the first was published in 2023, and the second which exemplifies the QbDD workflows using the 3 case studies has been prepared and will be submitted and we expect to be published in IJPX in 2025.

BENEFITS OF QBDD

- Improved efficiency and sustainability from digital-first and virtual assessments
- Ensures product Quality and consistency by combining patient-focussed quality targets with key manufacturing objectives and constraints, use of self-driving labs and standardisation of data

RESEARCH OUTCOMES

Key Papers

- Quality by Digital Design to Accelerate Sustainable Medicines Development: accepted by IJPX QbDD Special Issue https://doi.org/10.1016/j.ijpharm.2025.125625
- Quality by Digital Design: Exemplification of a Crystallisation and Isolation Workflow: will be submitted to upcoming combined IJP/IJPX special edition on Quality by Digital Design due for publication in 2025
- Digital Process Design to Define and Deliver Pharmaceutical particle Attributes: ChERD (DOI: http://dx.doi.org/10.1016/j.cherd.2023.07.003)

FLYERS

- Quality by Digital Design to Accelerate Sustainable Medicines Development - https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1ebda73d3c378c02b4ff/1745493697352/QbDD+Strategy.pdf
- Transforming Pharmaceutical Manufacturing with Quality by Digital Design – https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1df4bb58e75d29a07ba5/1745493497416/QbDD+Exemplar.pdf
- Exploiting Digital Tools for Pharmaceutical Quality Attribute And Process Design: Making Medicines More Sustainably - https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1ccfff-c8f95c46869faa/1745493201034/Exploiting%2Bdigital%2Btools%2Bfor%2Bpharmaceutical%2Bprocess%2Bdesign%2BFlyer%2BScreen.pdf

FURTHER FUNDING

- CEDAR (EP/Y035593/1)
- MediForge (EP/ Z532964/1)
- GiBio (EP/W036452/1)
- CERSI network (IUK 10113547)

Figure 8: QbDD Workflow

Crystallisation Classification System

AIMS:

- Define an informed User Requirement Specification (URS) for a CCS
- Develop a Crystallisation Classification System (CCS)

EXPECTED IMPACT:

- CCS capability enables in silico determination of process options and improves sustainability of pharmaceutical process development across the industry

The Crystallisation Classification System (CCS) is one of three model toolboxes referenced in the CMAC strategy 2021-26 (https://cmac.ac.uk/cmac-business-case-strategy) and on page p18-19 of this brochure. The three platforms span the production of primary particles to formulated product and address manufacturability, stability and performance, and – as part of Quality by Digital Design (QbDD) - provide an integrated framework leading to the digital transformation of CMC of pharmaceutical manufacturing. The CCS is designed to work alongside the materials classification system (MCS+) and the biorelevant performance classification system (BPCS), with a high level of interoperability (e.g. MCS+ and BPCS informing particle attributes for performance, stability and manufacturability and the CCS informing the process options to achieve these).

A roadmap to delivery showing how CCS focusses on going from molecule to particle has been co-created with the Hub Industry partners. The CCS will enable in silico process design using mechanistic, ML and hybrid models, and, through model-driven experimentation via DataFactories, continue to develop and improve these models. A three-phase development of the CCS has been proposed through working with the Hub Industry partners.

- Phase 1 delivered version 1 of the CCS predictive models and user interface as a Hub output
- Phase 2 will continue to develop models and interface with the DataFactories and MicroFactories in the MediForge programme.
- Phase 3 will identify gaps in current tools that require resources to develop through a planned series of workshops.

RESEARCH OUTCOMES

Flyer

- A Crystallisation Classification System to Accelerate Sustainable Medicines Development - https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1b1d45827e07cbbff86a/1745492768993/CCS.pdf

Further Funding

- PharmaCrystNet (EP/Z533014/1)

Other

- URS
- Model toolbox and user interface (version 1)

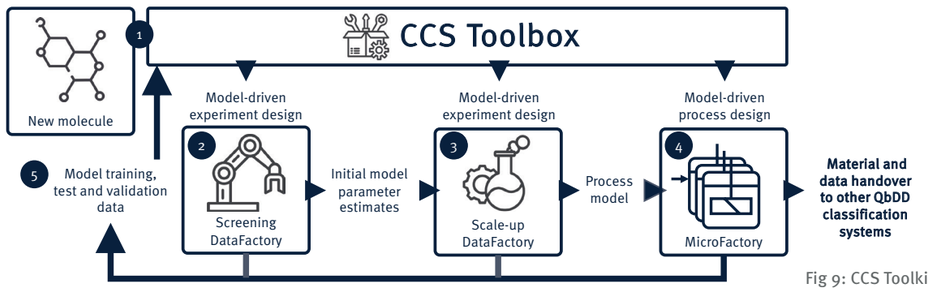


Fig 9: CCS Toolkit

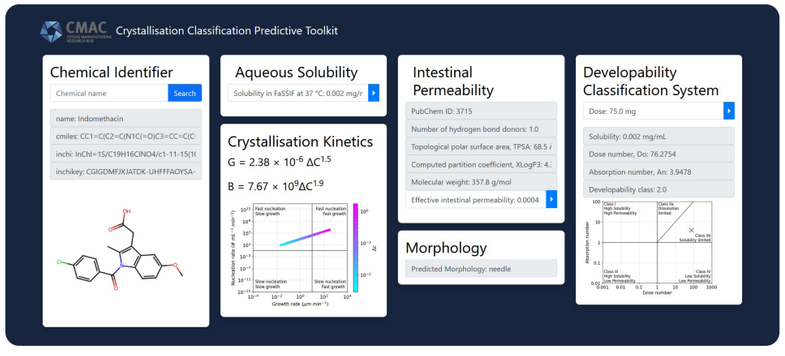


Figure 10: Example of CCS Version 1 interface for indomethacin, a non-steroidal anti-inflammatory drug

Crystallisation Screening DataFactory

AIMS:

- Model-driven workflows to cover all required data, parameters, models required by the Digital Twin for each stage of the process for >12 APIs
- Rapid data and turn around on >12 molecules

EXPECTED IMPACT:

- Creation of large, structured, Machine Learning-ready data sets for cooling crystallisation
- Furthering capabilities facilitates integrated data sets for isolation and morphology prediction of DataFactory APIs
- Round-the-clock experimentation will increase experimental output by 4x

To link the QbDD workflows explicitly to materials characteristics, an autonomous crystallisation and experimental data acquisition screening DataFactory (CSDF) was developed as part of the Hub. The CSDF informs the CCS and ultimately enables prediction of key material and process attributes from molecular descriptors and small-scale experiments. Once CSDF work on a particular API is completed, the solvent system and mode of crystallisation recommendations are taken forward to do initial parameter estimation in process models as per the QbDD workflow. The CSDF has seen successful integration of a dosing platform, robotic handovers, crystallisation platforms and real-time image analysis to enable high throughput data collection and has been demonstrated at the CMAC Open Days 2023, Hub Showcase 2024 and CMAC Open Days 2025.

RESEARCH OUTCOMES

Key Papers

- Rapid Assessment of Crystal Nucleation and Growth Kinetics: Comparison of Seeded and Unseeded Experiments: Cryst Growth Des (DOI: https://doi.org/10.1021/acs.cgd.2c01406)
- Developing a Model-driven Workflow for the Digital Design of Small-scale Batch Cooling Crystallisation with the Antiviral Lamivudine: CrystEngComm (DOI: https://doi.org/10.1039/D3CE00897E)
- Comparative Study on Adaptive Bayesian Optimization for Batch Cooling Crystallization for Slow and Fast Kinetic Regimes: Cryst Growth Des (DOI: https://doi.org/10.1021/acs.cgd.3c01225)
- Autonomous DataFactory: High-throughput Screening For Large-Scale Data Collection to Inform Medicine Manufacture: 13th APS PharmSci (DOI: https://doi.org/10.5920/bjpharm.1128)

Flyer

- A Crystallisation Screening DataFactory to Advance Medicines Manufacture - https://static1.squarespace.com/static/60ec00ca94dc0f2fa186098b/t/680a1b82e114373f3e12f10d/1745492870205/Crystallisation+Screening+DataFactory.pdf

Further Funding

- DDMAP (EP/W003295/1)
- CMAC Core projects on image analysis and scale up Crystallisation DataFactory
- Five PhD projects

Other

- The crystallisation screening DataFactory has produced two large datasets (Solubility Datasets for 16 APIs in 21 solvents from Crystallisation Screening DataFactory; Solubility + Kinetics Datasets for 10 APIs and 35 solvents from Crystallisation Screening DataFactory)
- PhD thesis [Thomas Pickles: Intensification of a workflow for particle engineering and crystallisation process development]
- Optimised methods and alpha version of CSDF platform

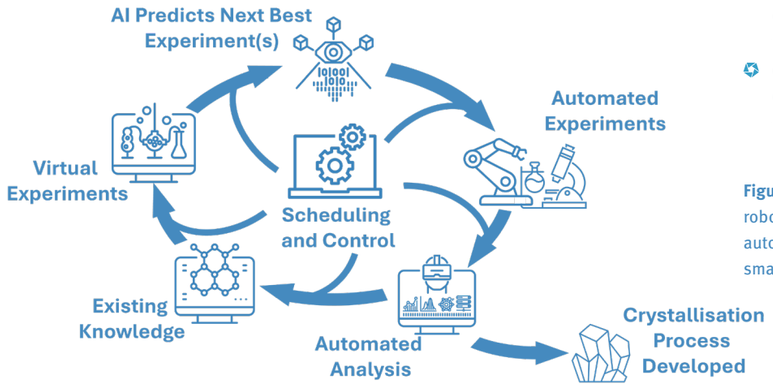


Figure 11: Integration of digital tools, robotics, and machine learning (ML) to automate the experimental workflow for small-scale batch cooling crystallisation

Digital Platform and Digital Twin Framework

AIMS:

- Digital Twin framework for Drug Substance
- An initial Drug Product Digital Twin
- Process models aligned with supply chain network models
- Workflows for smart experiments and advanced characterisation: capture domain knowledge
- Workflows for QbDD enabled Drug Substance and Drug Product process design

EXPECTED IMPACT:

- Improved capability: models, prediction, classification, ICT tools
- Use of Digital Twins to drive MicroFactory process design, operation and control

The Digital Twin work in the Hub included design of the integrated digital framework to collate, analyse, visualise and apply data, models and knowledge. This included rapid design, control, operation and testing of continuous processes for Drug Substance crystallisation and Drug Product production in the DataFactory and MicroFactory platforms. The Digital Twin framework is supported by the broader digital platform enabling the team to take a structured and systematic approach to embedding data and model driven methods across the programme.

The Digital Twins combined the overarching digital definition of processes and products. For example, the team used the QbDD workflows to gather data and inform model development, optimisation and implementation. These data, models and knowledge were then captured, stored and interrogated in the Digital Twin framework. The QbDD workflow develops a specific Digital Twin for a particular Drug Substance process and product.

In Phase I the Hub team created a suite of workflows and models for various rate processes for crystallisation, filtration and direct compression processes.

The team also expanded capability in predictive models for morphology by creating an Additive Workflow, doing design and assessment of additive intervention for morphology improvement and control. The team also created a Co-crystal workflow. They integrated ADDoPT Tools, and implemented CCDC tools, and created additive processes for making Drug Substance.

The Hub expanded capability in predictive models for solubility and solvent selection by creating workflows, developing predictive models of solubility using the SAFT-g Mie group contribution equation of state, developing a computer-aided molecular and blend design (CAMbD) framework for solvent selection, and advancing in the underpinning theory, creating new group-group interaction parameters for SAFT-g Mie, and a framework for solvent design. The team has created and populated a digital library called AssetStore.

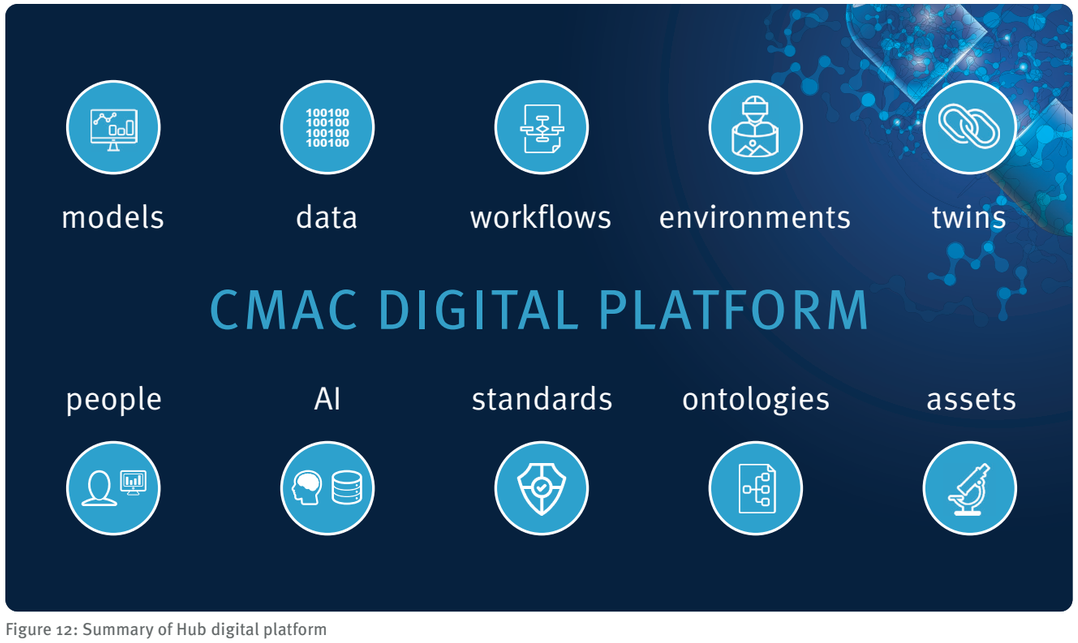


Figure 12: Summary of Hub digital platform

ASSETSTORE POPULATED WITH HUB ASSETS:

Category	Description of Asset
Quality by Digital Design	QbDD BPMN processes in bpmn and image formats (V1 & V2)
	QbDD workflows internal report, Supporting items for QbDD Strategy Paper
Crystallisation Screening DataFactory	2 large datasets from Crystallisation Screening DataFactory
	2 models: image analysis and optimisation for Crystallisation Screening DataFactory experimental
	CAD Drawings of CSDF automated workflow equipment
	BPMN of Crystallisation Screening DataFactory experimental workflow , and pseudoseeding workflow
Digital Platform and Digital Twin Framework	CMAC Digital Twin App - Open Day 2022
	Process models for Ibuprofen, Lamivudine and proprietary compound used to exemplify the QbDD workflows in Phase II of the Hub Programme
	Many-Objective Optimisation Model for Tableting and Dissolution Testing of Lovastatin
	gPROMs Import and Export Tools
	Integrated Isolation and filtration gPROMS models
	Global System Analysis Modelling of Mefenamic Acid Continuous Crystallization
	AI Prediction of pharmaceutical crystal morphology
	AI Enhanced Solubility Model
	CrystalEyes
	Powder Prediction models
MicroFactories	URS for API Test bed used in CMAC Hub Phase II
	MSMPR PharmaMV Dashboard
Spherical Agglomeration	SA models and workflow from CMAC Hub Phase I
Advanced Characterisation	Advanced characterisation workflow
	Analytical workflow (BPMN)
	Crystal Growth Tracker to analyse crystal face advancement rates from time lapse synchrotron radiography

In Phase II the Hub worked on an integrated approach to "Digital-first" for crystallisation process development and QbDD as described on pages 28-29. The team developed the AssetStore and populated it with 33 digital assets that are outputs from the Hub.

RESEARCH OUTCOMES

Key Papers

- Tuning Morphology in Active Pharmaceutical Ingredients: Controlling the Crystal Habit of Lovastatin through Solvent Choice and Non-Size-Matched Polymer Additives: in Cryst Growth Des (DOI: https://doi.org/10.1021/acs.cgd.0c00470)
- Linked Experimental and Modelling Approaches For Tablet Property Predictions: in IJP (DOI: https://doi.org/10.1016/j.ijpharm.2022.122116)
- Computer-aided Solvent Mixture Design for the Crystallisation and Isolation of Mefenamic Acid: in Computer Aided Chemical Engineering (DOI: https://doi.org/10.1016/B978-0-12-823377-1.50109-9)
- Digital Design of Filtration and Washing of Active Pharmaceutical Ingredients via Mechanistic Modeling : in OPRD (DOI: http://dx.doi.org/10.1021/acs.oprd.2c00165)
- A Unified ML Framework for Solubility Prediction Across Organic Solvents: in Digital Discovery (DOI: http://dx.doi.org/10.1039/D2DD00024E)
- Computer Aided Design of Solvent Blends for Hybrid Cooling and Antisolvent Crystallization of Active Pharmaceutical Ingredients: in OPRD (DOI: http://dx.doi.org/10.1021/acs.oprd.0c00516)
- Predicting Pharmaceutical Powder Flow From Microscopy Images Using Deep Learning : in Digital Discovery (DOI: http://dx.doi.org/10.1039/d2dd00123c)

Further Funding

- ARTICULAR (EP/R032858/1)
- DM2 (EP/V062077/1)
- KTP with Siemens
- 7 PhD projects (Strathclyde)

Other

- AssetStore and 33 digital assets summarised in table above
- 5 PhD Theses (3 at Strathclyde, Imperial and Loughborough)

MicroFactories

AIMS:

- Working MicroFactories: innovative flexible efficient production systems comprising integrated processing platforms
- New and improved process development technology

EXPECTED IMPACT

- Accelerated development of product and optimised manufacturing processes
- Validation of model approach and identification of impact of non-modelled phenomena
- Rapid prototyping capability to control, measure and optimise critical transformations across multiple length-scales spanning crystal and particle engineering, structured product and dosage form generation
- Managing variable material properties and increased product complexity
- Improved capability

DRUG SUBSTANCE

The Drug Substance MicroFactory test bed is now comprised of a MSMPR which can operate in batch or continuous mode with feed and seed vessels and is designed for flexibility in terms of number of vessels, sizes, residence times and slurry transfer approaches. Several filtration, washing and drying units are installed including an AWL CFD25 semi-continuous carousel filter. PAT-enabled control allows control of Critical Quality Attributes (CQAs) in real time.

Improved Capabilities

- Energy efficient Huber circulators installed through Net Zero RPIF funding – 60% less power consumption and energy savings equivalent to approx. 530kg CO_2 per year
- Fixed lid configuration, variable vessel size with rapid interchange (250-5000ml) provides process flexibility and large design space
- Dashboards developed for real-time monitoring process and PAT
- Closed-loop supersaturation control using in-line PAT
- Increased slurry transfer options including periodic pressure transfer to improve robustness reducing blockages and down-time

QbDD Workflow Exemplification

The Hub team implemented the QbDD framework on three exemplar APIs - Ibuprofen, Lamivudine and a proprietary compound - on the Drug Substance platform. This work has underpinned a forthcoming paper that demonstrates the application of the QbDD framework for drug manufacture. The paper is titled Quality by Digital Design: Exemplification of a Crystallisation and Isolation Workflow will be submitted to upcoming combined IJP/IJPX special edition on Quality by Digital Design due for publication in 2025

Drug Substance MicroFactory Achievements

- Processes for API manufacture of mefenamic acid, ibuprofen, lamivudine and proprietary API developed using QbDD framework
- Lovastatin drug substance platform for crystallisation and spherical agglomeration, lovastatin process Intensification completed
- Modular API MSMPR MicroFactory assembled, PCS7 control system, URS for MSMPR updated and platform modified

Image: Stage MSMPR setup with intermittent pressure driven transfer running Ibuprofen cryst.

RESEARCH OUTCOMES

Key Papers

- Integrated Continuous Process Design for Crystallisation, Spherical Agglomeration, and Filtration of Lovastatin: in J Pharm Innov (DOI: https://doi.org/10.1007/s12247-024-09815-z)
- Engineering of acetaminophen particle attributes using a wet milling crystallisation platform: in IJP (DOI: https://doi.org/10.1016/j.ijpharm.2018.10.073)
- Enabling precision manufacturing of active pharmaceutical ingredients: workflow for seeded cooling continuous crystallisations: in MSDE (DOI: https://doi.org/10.1039/C7ME00096K)
- Developing a Batch Isolation Procedure and Running It in an Automated Semicontinuous Unit: AWL CFD25 Case Study: in OPRD (DOI: https://doi.org/10.1021/acs.oprd.9b00512)

Further Funding

- SoLViT (EP/ W01923X/1)

Other

- PhD Thesis

DRUG PRODUCT

The Drug Product MicroFactory manufacture is carried out via polymer processing using extrusion-3D printing technologies. A novel, filament-free fused deposition modelling printer has been developed in-house, opening up the pharmaceutical formulation space in this area. The Hub team have also use filled capsules to develop a fully integrated Digital Twin spanning drug substance, drug product and performance testing.

Benefits

- This platform reduces material used to identify optimal process
- Challenging formulations can be accessed
- Streamlines the process by integrating unit operations of HME and printing
- Fabrication step is eliminated

RESEARCH OUTPUTS

Key Papers

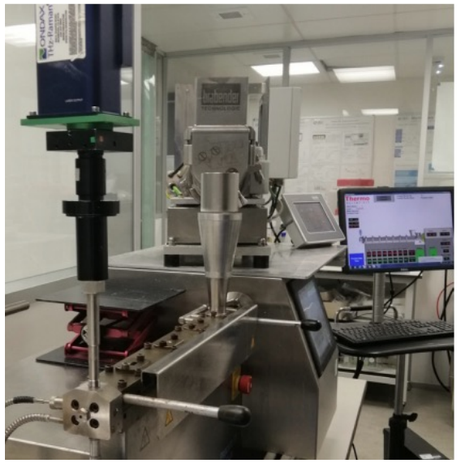
- An Additive Manufacturing MicroFactory: Overcoming Brittle Material Failure and Improving Product Performance through Tablet Micro-Structure Control for an Immediate Release Dose Form: Polymers (DOI: https://doi.org/10.3390/polym16182566)
- Expanding the pharmaceutical formulation space in material extrusion 3D printing applications: Additive Manufacturing (DOI: https://doi.org/10.1016/j.addma.2023.103803)
- Mefenamic acid solid dispersions: Impact of formulation composition on processing parameters, product properties and performance: IJP (DOI: https://doi.org/10.1016/j.ijpharm.2022.121505)

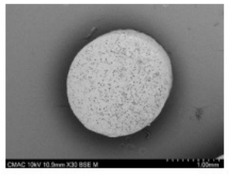
Further Funding

- MMIC GC1
- DDMAP (EP/W003295/1)
- DM2 (EP/V062077/1)
- Dialling up performance for on demand manufacturing (EP/W017032/1)
- Pressure dependent In-Situ Monitoring of Granular Materials (EP/S02168X/1),
- RiFTMaP (EP/V034723/1)
- Six PhD projects (5 at Strathclyde, 1 at Sheffield)

Other

- Two PhD theses
- Core project on compaction
- Novel combined Hot Melt Extruder and 3DPrinter unit -patent granted, Adaptimed spin out in late stages of formation





50% MFA + Soluplus + 15% Sorbitol, SEM image of extrudate face (above, top) and photograph of filament extrudate (above, bottom)

Image: Integrated 3D printer and Hot melt extruder platform.

Spherical Agglomeration

AIMS:

- Spherical Agglomeration models and process understanding improved

EXPECTED IMPACT:

- Controllable, predictable particle engineering processes with improved process understanding

In Phase I the team at University of Sheffield developed capability in Spherical Agglomeration by developing population balances models and a microfluidic device for manufacturing of tuneable spherical agglomerates. They published a Mechanistic description for spherical agglomeration, and generated mechanistic understanding of the Spherical agglomeration process. Digital assets from this work include:

- Model that describes the kinetics of the immersion nucleation mechanism of spherical agglomeration
- True Binder Solid Ratio parameter
- Population balance model for spherical agglomeration (gPROMS)
- Spherical Agglomeration workflow for rapid development

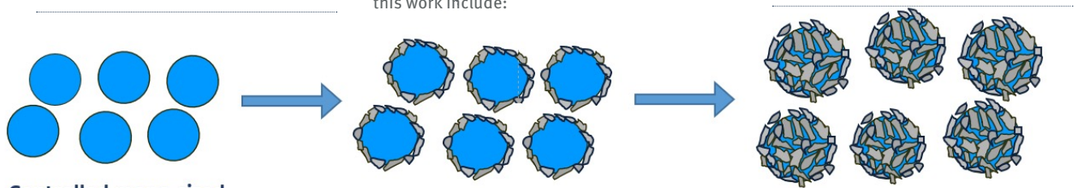


Figure 13: Spherical agglomeration mechanism

RESEARCH OUTPUTS

Key Papers

- A New Mathematical Model for Nucleation Of Spherical Agglomerates By The Immersion Mechanism: in Chemical Engineering Science X (DOI: https://doi.org/10.1016/j.cesx.2019.100048)
- Particle Design Via Spherical Agglomeration: A Critical Review of Controlling Parameters, Rate Processes And Modelling: in Powder Technology (DOI: https://doi.org/10.1016/j.powtec.2017.11.052)
- True Bridging Liquid-Solid Ratio (TBSR): Redefining A Critical Process Parameter in Spherical Agglomeration: in Powder Technology (DOI: https://doi.org/10.1016/j.powtec.2023.119010)
- Spherical Agglomeration Kinetics: A Mechanistic Approach: in Powder Technology (DOI: https://doi.org/10.1016/j.powtec.2024.120082)

Further Funding

- CMAC Core project on Spherical Agglomeration

Drug Product Performance Model Capability

AIMS:

- Develop new models that describe and predict the performance of OSDs

EXPECTED IMPACT:

- Drug Product Performance capability advanced

The link between the internal microstructure of drug products and the performance of Oral Solid Dosage forms (OSDs) is complex, and research in this area is vital for the development of predictive tools to enable design of manufacturing processes for desired product performance.

In CMAC Hub phase II mechanistic models have been developed to describe important rate processes driving OSD dispersion, dissolution and disintegration. Also novel characterisation techniques such as optical coherence tomography (OCT) have been employed to visualise evolving OSD microstructure over time. The recent work has been focused on model development, experimental validation techniques and the implementation of models into existing and in-development model platforms for OSD manufacture.

RESEARCH OUTPUTS

- gPROMS models, PhD thesis (Sheffield)
- Poster and showcase demonstration in CMAC Open Days 2023: Mechanistic Modelling of Disintegration Mechanisms for harmaceutical Products (Bala et al)
- Poster in Hub Showcase 2024: Model Assisted Design of Pharmaceutical Products: Linking Process and Performance Models for Formulated Products (Smith et al)

Supply Chain

AIMS:

- New production and supply network configuration design options and strategies aligned with emerging production process technologies advanced production process control and analytics
- Integration of end-to-end supply chains enabled by ICT/digitalisation
- Operational and Product benefits from Continuous Manufacturing
- MicroFactory based Continuous Manufacturing system models
- Whole system design tools

EXPECTED IMPACT:

- Maximize the impact of continuous manufacturing to enable new product sourcing and distribution paradigms, focused on targeting demand at differing scales in response to changing consumer or patient expectations
- Use of Digital Twins to drive MicroFactory design, operation and control

Image: Packaged tablets

The Supply chain research provideda multidisciplinary approach to the early assessment of manufacturing network reconfiguration opportunities enabled by advanced manufacturing technology concepts developed within the Hub. The supply chain workflow is aligned with the QbDD workflow. Opportunities for advanced manufacturing technology interventions in commercial pharmaceutical supply chains were identified and assessed through a supply chain reconfiguration lens relative to the current state. To do so, the team have developed methodologically diverse, yet complementary types of analysis:

- Informing molecule & technology selection based on managerial and engineering principles
- Structuring expert judgment on targeted technology interventions by structural modelling techniques facilitated by digital apps
- Evaluating opportunities for advanced manufacturing and digital infrastructure investment

Published research from this work demonstrates how digital supply network design tools can inform the multi-disciplinary evaluation of alternative pharmaceutical supply network configurations enabled by MicroFactory technologies.

Research areas include:

- Interventions and the associated network configuration options for specific therapeutic areas
- Investment in digital infrastructure and manufacturing capabilities that enable supply resilience

RESEARCH OUTCOMES

Key Papers

- Continuous Manufacturing Technologies In Upstream Pharmaceutical Supply Chains: Combining Engineering And Managerial Criteria: in Journal of Multi-Criteria Decision Analysis (DOI: https://doi.org/10.1002/mcda.1775)
- Where Have All The Equations Gone? A Unified View On Semi-Quantitative Problem Structuring And Modelling: in Journal of the Operational Research Society (DOI: https://doi.org/10.1080/01605682.2022.2039565)
- Emerging Applications and Regulatory Strategies for Advanced Medicines Manufacturing - Towards the Development of a Platform Approach: in J Pharm Sci (DOI: https://doi.org/10.1016/j.xphs.2024.04.016)
- Evaluating the Business Case for Continuous Manufacturing of Pharmaceuticals: A Supply Network Perspective: in Continuous Pharmaceutical Processing (DOI: https://doi.org/10.1007/978-3-030-41524-2_14)
- Settanni et al 2018, https://www.teknoscienze.com/tks_article/towards-a-new-approach-to-modellingpharmaceutical-supply-chains-in-achanging-technological-landscape/)

Further Funding

- DM2 (EP/V062077/1)
- Innovate UK Smart Pharma Supply Chains

Other

- Supply Chain workflow
- Supply Chain Configuration Tool for evaluating CMAC technology interventions
- Prototype tools demonstrated at CMAC Open Days 2023

Advanced Characterisation

AIMS:

- Establish and develop analytical methods to track evolution of structure and properties for critical material, process and quality attributes
- Develop platform units and workflows for advanced characterisation for unit operations
- Demonstration how structure data can be integrated with QBDD
- Advanced Measurements capability increased
- Proposals, collaborations, partnerships developed

EXPECTED IMPACT:

- Advanced characterisation capability advances across length scales from the molecule to the particle to inform process design

The Advanced Characterisation work done on the Hub seamlessly integrated research with advanced analytical instruments at UK national facilities such as Diamond Light Source and the Henry Royce Institute with a multi-institution laboratory presence on the UK Science and Innovation Campus at Harwell.

One highlight of Hub research has been the development of a synchrotron X-ray pair distribution function (XPDF) methodology that produces experimentally validated molecular structure models for solutions and solvents. The resulting understanding of the relationships between phase behaviour, thermodynamic properties and molecular structure is now paving the way for predictive methods allowing rational choice of solvent mixtures in solvent selection. Real-world manufacturing impact is being created through a deep multi-scale understanding of the molecular basis for crystal nucleation events in solutions. This has led to quantitative design and modelling techniques based on the nucleation dynamics associated with local density fluctuations in solutions, linking in molecular de-solvation and solute pre-ordering processes for targeted product properties.

Hub research has driven the development of an absolute rate theory for homogeneous nucleation from solution, which integrates Drug Product Performance Models (Sheffield), the influence of supersaturation, solubilities and temperature through a straightforward mathematical framework that is amenable to real-time process modelling and control.

Another example of advanced characterisation research in the Hub has been the development of real-time X-ray phase contrast imaging (XPCI) of crystallisation processes with synchrotron radiation. XPCI visualises the microscopic loci of crystal nucleation and permits real-time determination of crystal size distributions and morphologies. Finally, we have pioneered the use of environmental X-ray photoelectron spectroscopy (XPS) in the Henry Royce Institute for determining the impact of surface composition, speciation and phase behaviour in non-crystalline and crystalline forms.

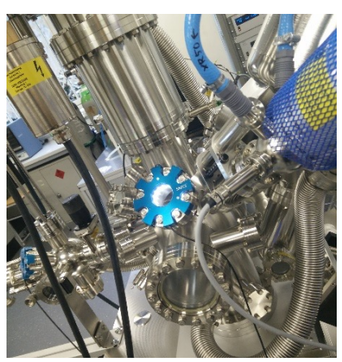
RESEARCH OUTCOMES

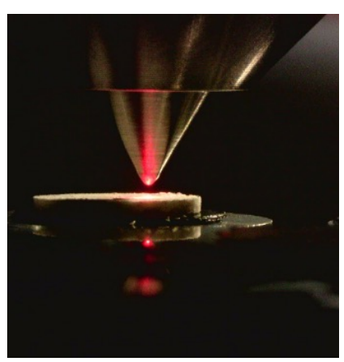
Key papers:

- X-ray Raman Scattering: A New In Situ Probe Of Molecular Structure During Nucleation And Crystallization From Liquid Solutions: in CrystEngComm (DOI: https://doi.org/10.1039/C8CE00929
- Dynamic Crystallization Pathways of Polymorphic Pharmaceuticals Revealed in Segmented Flow with Inline Powder X-ray Diffraction: in Analytical Chemistry (DOI: https://doi.org/10.1021/acs.analchem.0c00860)
- In situ non-invasive Raman spectroscopic characterisation of succinic acid polymorphism during segmented flow crystallisation: in Molecular Systems Design & Engineering (DOI: http://dx.doi.org/10.1039/C9ME00103D)
- Bulk and Surface Conformations in Solid-State Lovastatin: Spectroscopic and Molecular Dynamics Studies: in Crystals (DOI: https://doi.org/10.3390/cryst11050509)
- Homogeneous Organic Crystal Nucleation Rates in Solution from the Perspective of Chemical Reaction Kinetics: in Crystals 2024 (DOI: https://doi.org/10.3390/cryst14040349)

Further Funding

- EPSRC -Flow XI (EP/T006331/1)
- SAXS/WAXS Facility (EP/ R042683/1





Images: Advanced characterisation techniques

Impact

Now that the CMAC Hub has completed its research programme, we expect impact to be generated from application of our research outputs in the wider community including our industry partners. In addition, follow up programmes will enable next generation digital and advanced medicines manufacturing approaches.

Quality by Digital Design & Digital Workflows

Two papers will be published in IJPX Special Edition on Quality by Digital Design in 2025. QbDD strategy, workflows and exemplification of the approach are covered. The publication on QbDD Strategy has been co-authored by our industry partners, and we expect both papers to be highly relevant to them, as well as the wider community, with potential to deliver impact there. This work helped with achieving further funding of the CERSI project that kicked off in 2025 where the aim is to help regulators to use this new approach to streamline the regulatory process for new medicines. The impactful framework and ambitious vision also have informed new research and training activities through the award of an ESPRC CDT for Cyber-Physical systems for Medicines Development and Manufacturing (CEDAR) and EPSRC MediForge Manufacturing Hub for a Sustainable Future.

DataFactories & Model-driven Experiments

Work on the crystallisation screening DataFactory (CSDF) has delivered a step change in data generation to support development of a Crystallisation Classification System (CCS) that was co-created by CMAC and our partners. The initial development and capability will be expanded in the new MediForge Hub to create end-to-end cyberphysical systems that can generate substantial new data sets to drive digital transformation of CMC. This will also help deliver Industry 5.0 goals of sustainability, resilience and human-centricity to the community.

Data and Digital Twins

The Hub team has published extensively on data and digital assets developed during the project. The AssetStore internal database developed in the Hub as a way of capturing developments has 33 digital assets uploaded, and 25 are from CMAC Hub work. The CMAC Industry team have recorded the number of technologies translated to industry that have delivered demonstrable impact and is working with industry to develop a sustained pipeline of translation to industry projects for the most promising tools. In March 2024 we reported to the CMAC Advisory Board that 24 assets had been translated since start of 2022 with 119 assets in portfolio. At the end of the project 126 portfolio assets had been recorded.

MicroFactories & Advanced Process Technology

The Hub's MSMPR platform, designed and applied across the Hub research has delivered considerable learning in the modelling, operability and optimisation of these platforms. This work will contribute to increased adoption through more robust processes. Secondary Processing filament-free printer platform developed in CMAC during the Hub project has had a patent granted and the University of Strathclyde is exploring ways to commercialise the technology. Our MicroFactories vision developed through the CMAC Hub has contributed to advances in the integration of process technologies, PAT and digital technologies as part of our digital first approach. In drug substance processing, this has led to advanced discussions with the MMIC to develop a pilot scale demonstrator for integrated continuous crystallisation, isolation and drying (CCID) as well as a second-generation research test bed design that has been funded via our UKRPIF Data Lab. This will form a key strand in future funded programmes including EPSRC MediForge Hub and CEDAR CDT.

Figure 14: Four research goals in CMAC Strategy

CMAC Future Manufacturing Research Hub Overview

Date	Item
January 2017	CMAC Future Manufacturing Research Hub Started
March 2017	CMAC Open Days 2017
2017	Visit by Lord Duncan of Springbank, Parliamentary Undersecretary of State in the Scotland Office
2017	Visit by AZ Senior Team
December 2017	Pfizer becomes a CMAC Tier 1
June 2018	Visit by ministers (Lord Duncan (Parliamentary Under Secretary of State for Scotland) and Paul Wheelhouse (the Scottish Government Minister for Business, Innovation and Energy)
August 2018	Ministerial visit by Ivan McKee (Minister for Trade, Investment & Innovation) and Sam Gyimah MP (joint Minister for Higher Education at the Department for Business, Energy and Industrial Strategy and the Department for Education)
September 2018	Visit by UK Chancellor of the Exchequer, Philip Hammond
October 2018	ISCMP 2018
November 2018	CMAC Open Days 2018
January 2019	Scottish Science Advisory Council (SSAC) Reception
May 2019	CMAC Industry Showcase US
October 2019	CMAC Industry Showcase UK
October 2020	CMAC Virtual Open Days 2020
February 2021	Mid-Term Review and start of Phase II
February 2021	Virtual ISCMP 2021
November 2021	Visit by Dame Ottoline Leyser, CEO UKRI
June 2021	Online Mini Symposia for Industry and CMAC PhDs
June 2021	An impact story and film featuring CMAC was on the front page of the UKRI website
September 2021	DM2 Project started
November 2021	CMAC 10 years old and launch Strategy 2021-2026
February 2022	Queens Anniversary Award 2022
February 2022	Visit by Paul Scully, Parliamentary Under Secretary of State (Minister for Small Business, Consumers & Labour Markets)
February 2022	Visit by UK Science and Technology Select Committee
April 2022	CMAC London office opens
May 2022	CMAC Open Days & Articular Showcase 2022
June 2022	CMAC REF 2021 submission published
July 2022	Visit by Lord Offord, Parliamentary Under Secretary of State to the Scotland Office
September 2022	CMAC participate in Doors Open Glasgow
January 2023	EPSRC 's Executive Chair, Lynn Gladden visit & blog mention
May 2023	Visiting Professors Engaged
March 2023	Version 1 of QbDD Workflow mapped
November 2023	Bronze LEAF Award to CMAC National Facility
April 2023	ICAMM 2023 & CMAC US Roadshow
August 2023	Digital First approach published
September 2023	ISIC 2023
November 2023	CMAC Open Days 2023
April 2024	Visit from Bahrain Health Sector
April 2024	CEDAR CDT started
August 2024	DPN-MED and SHARPEN projects started
August 2024	Version 2 of QbDD Workflow mapped
August 2024	Visit from Department for Business and Trade
September 2024	Anas Sarwar (Leader Scottish Labour Party)
September 2024	CMAC Future Manufacturing Research Hub Showcase
30th September 2024	Project Closed
1st October 2024	MediForge Project started
1st November 2024	CERSI Project started

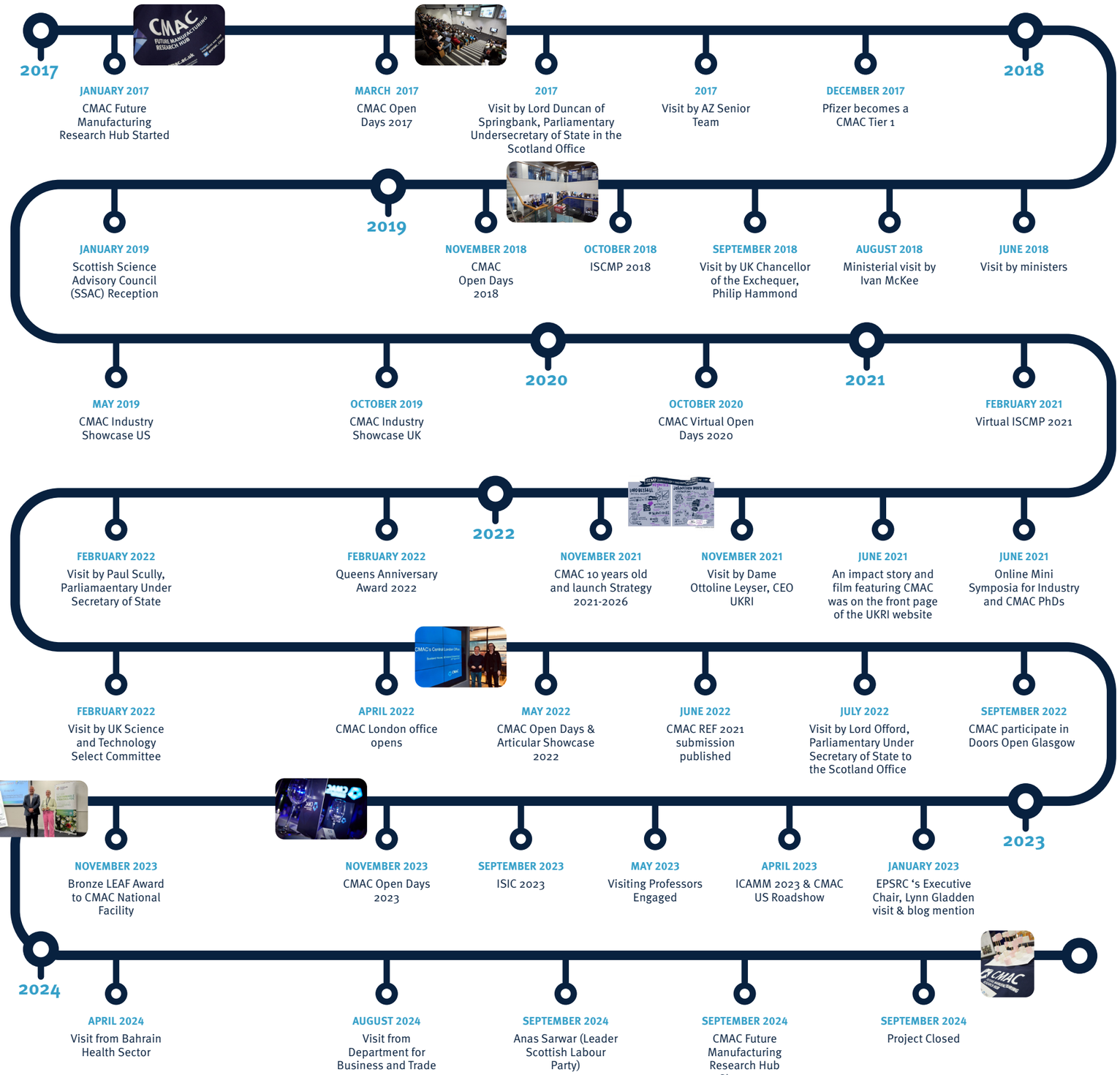


Figure 15: Hub timeline

MediForge

Industry 5.0 Medicines Manufacturing Research Hub

MEDIFORGE IS AN EPSRC MANUFACTURING RESEARCH HUB FOR SUSTAINABLE FUTURES PROGRAMME CO-CREATED THROUGH COLLABORATION BETWEEN WORLD-RENOWNED ACADEMIC AND INDUSTRY EXPERTS.

HUB VISION:

MediForge will pioneer an Industry 5.0 manufacturing system paradigm for sustainable, resilient, and human-centric medicine manufacture.

DRIVERS:

- Meet the demand for affordable sustainable healthcare
- Accelerate patient access to new medicines
- Assure the resilient supply of quality medicines
- Address the climate crisis and reaching Net Zero goals
- Enable the workforce of the future

TEAM:

Our strong industrial (AZ, Chiesi, Lilly, Pfizer, Roche, Sanofi, Takeda, UCB, Applied Materials, Bruker, CCDC, Clairet, digiM, MStar, Siemens, Tecnobis, ULab, CPI, NMIS) and academic (Universities of Strathclyde, Leeds, Sheffield, Glasgow School of Art, Imperial College London) team in MediForge builds on a successful track record of 10+ years engagement and research partnerships. The programme will be delivered via a Hub and Spoke model. Together we will create a distinctive, globally-leading MediForge Hub to positively impact medicine manufacturing practice.

MediForge will deliver the research to pioneer an Industry 5.0 manufacturing system paradigm for sustainable, resilient, and human-centric medicine manufacture via 5 Platforms. The programme will embed sustainability goals in all Platforms to address the environmental impact of medicines manaufacturing and also the impact of the Mediforge Hub operations.

MediForge has begun to establish itself as a Global Hub providing International leadership in the research, development and innovation community to drive the transformation of Industry 5.0 medicines manufacturing and modernisation of CMC procedures.

Figure 16: MediForge Global Hub

The programme will run in 2 phases. Phase I is running from October 2024. We have, with our partners, identified two initial areas of Chemistry Manufacturing and Control (CMC) where significant benefits can be achieved by integrating challenging multi-component, multi-phase sub-systems and are working towards delivering these by end of year 4.

Overarching Research Objectives for Phase I:

- CMC Objective I – simultaneous design and optimisation of synthesis, purification and isolation for Drug Substance manufacture
- CMC Objective II - simultaneous design of innovative Drug Substance co-processing routes and oral solid dose form production

Addressing these objectives will help to meet the following challenges:

- New understanding and insights into the intricate interactions between process stages
- Improved design and operation of sustainable, cost-effective manufacturing processes
- Standardise protocols and approaches help deploy CPRI for accelerated process development
- Confront the challenges in capturing and sharing FAIR data for research and translation
- Address competing multiple objectives in early-development, maximising benefits across the product life cycle
- Bridge the skills gap that inhibits organisations' ability to adopt advanced technologies and innovate
- Realise translation pathways for research outputs and mechanisms to work across the RDI system
- Bring to the international medicine manufacturing community inclusive ways to implement responsible regulatory change for the digital transformation of CMC

In Figure 17, the Learn platform integrates data from experiments across multiple process stages and uses it to feed into the research data fabric.

The Model platform creates a systems-level manufacturing knowledge model for CMC, integrating predictive models into an E2E model framework to inform knowledge management.

The Make platform is a lab scale, customizable manufacturing test bed to validate quality, sustainability, and resilience of processes and control strategies, developing processes designed in the Model platform.

The Adapt platform includes multi-skilled researchers working in a diverse and inclusive environment for medicine manufacturing innovation).

Figure 17: Image highlighting CMAC's additionality between Data Lab, CEDAR CDT and MediForge Hub in developing integrated cyber-physical infrastructure

Platform 1: Learn

The goal for Platform 1 is a step change in fundamental understanding across the end-to-end medicines manufacturing value chain from synthesis to formulated drug product. It will address the interfaces between key unit operations through the creation of a novel human-centric Cyber Physical Research Infrastructure (CPRI) and a research data fabric.

TO BE ACHIEVED BY:

- Developing CPRI capability
- Multi-objective optmisation across multiple integrated unit operations
- Develop and apply extract, transform and load (ETL) pipelines to capture all relevant data from CPRI, simulations and test beds

DESIRED OUTPUTS:

- 10-fold increase in productivity, up to 60% reduction in material use and waste and increased reproducibility and accuracy
- The world's largest E2E medicines manufacturing research data fabric covering: physicochemical and structural properties; kinetic and process data, and sustainability metrics
- Automated, closed-loop, sustainable process designs for CMC I and CMC II objectives
- Standard architecture for medicines manufacturing CPRI and lifecycle model
- Sustainability: 60% reduction in raw material with impact on energy use and waste generation
- Resilience: Robust cybersecurity of data fabric and FAIR data management; transferable, scalable technology adoption
- Human-centricity: Reduction of repetitive tasks freeing researchers for creative tasks (90%); intelligent decision support

Image: Crystallisation Screening DataFactory

Image: Tabletting DataFactory

Platform 2: Model

The goal for Platform 2 is the development of a new system-level manufacturing knowledge model for Chemistry, Manufacturing and Controls (CMC) with a real-time Digital Twin to model, optimise and accelerate end-to-end process selection and design with embedded sustainability objectives.

TO BE ACHIEVED BY:

- Developing an end-to-end model framework for a real-time Digital Twin capability
- Developing new models to fill current capability gaps
- Optimising parameters for robust product design space, with embedded life-cycle analysis
- Creating a knowledge model and ontology for end-to-end medicine manufacturing

The outputs from this platform include smarter, data-driven models capable of designing new manufacturing routes, optimising product quality, and achieving environmental targets. These tools will not only accelerate the delivery of life-saving medicines to patients but also pave the way for a future of sustainable and human-centric pharmaceutical production. Through collaboration with other platforms, P2 Model will help create an interconnected modelling ecosystem, showcasing the immense potential of digital innovation in reshaping medicine manufacturing

DESIRED OUTPUTS:

- System of models and workflows
- Reverse engineering solvent selection across multiple unit operations
- Reverse engineering for spherical co-agglomeration control of bulk properties
- Generative AI process design and orchestration for optimal manufacturing route
- LCA and sustainability measures of optimised process designs, including carbon costs of all computing
- Sustainability: Reduction of: waste arising from production of off-spec material (>50%), premature stock wastage (50%)
- Resilience: Increased agility through robust and adaptable model framework
- Human-centricity: Enable researchers to quickly visualise data, customise workflows, and leverage simulations with a location-agnostic knowledge model

Image: Bringing Digital Twins into the Lab of the Future

Platform 3: Make

The goal for Platform 3 is to create an integrated, scaled-down, material-sparing end-to-end customisable manufacturing research test bed to translate and link the outputs from platforms 1 and 2 and validate the quality, sustainability and resilience of adaptive processes, and control strategies.

TO BE ACHIEVED BY:

- Integrate a CMC I Test Bed (Synthesis to drug substance to drug product with impurity management)
- Integrate a CMC II Test Bed(co-processed drug substance to drug product)
- Integrated end-to-end (E2E) Test Ted for CMC I and CMC II
- Assess predictive performance of Digital Twin by running the process designs
- Identify further data and knowledge model requirements to improve model capabilities
- Assess control strategies

DESIRED OUTPUTS:

- An agile E2E medicines manufacturing platform and data
- Automated model verification and validation in (near) real-time
- AI-based process analytics and control strategies
- Sustainability: Reduction of stock write-offs for clinical trials (50%)
- Resilience: Adaption of processes in real-time
- Human-centricity: Instant predictions from models served through extended reality (XR) technologies to guide in-lab decision-making

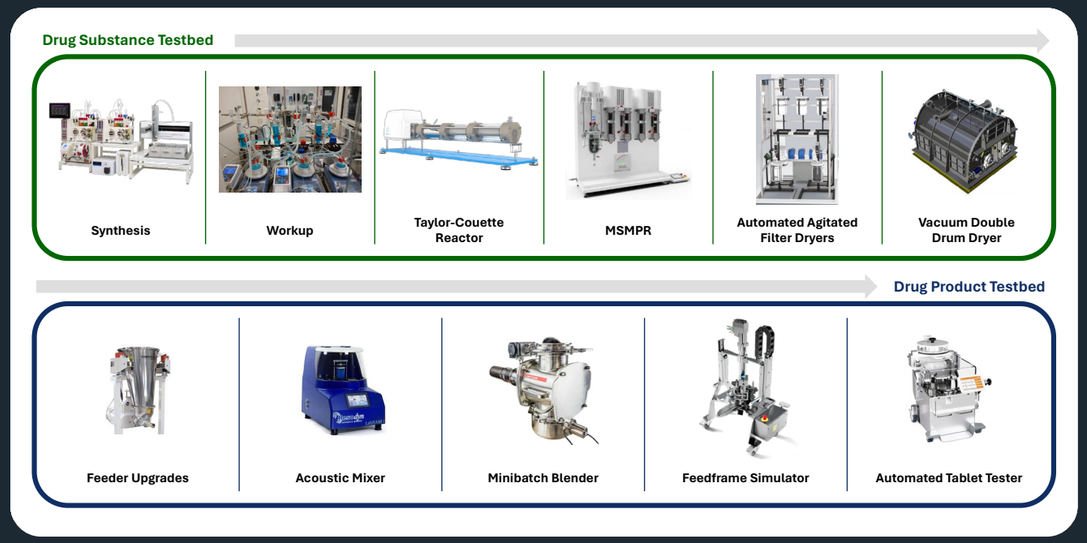


Figure 18: Test Bed equipment

Platform 4: Adapt

The goal for Platform 4 is to create a Living Lab environment. It will be an open innovation ecosystem for researchers, industry partners, heathcare providers and regulatory bodies to collaborate, co-create, test, validate, and scale-up processes, technologies and products. This will create a diverse and interdisciplinary team, skilled in Industry 5.0.

TO BE ACHIEVED BY:

- Creating a Living Lab with interactive immersive environments
- Establishing an interdisciplinary collaborative research culture embedding Industry 5.0 aims
- Providing the team with the tools and skills needed to succeed
- Driving agility, data and model sharing across sites and platforms
- Engaging with partners to define sustainability, resilience and human-centric metrics across all platforms.
- Enabling efficient data and knowledge management delivery

SKILLS

CMAC SkillsFactory has been established by the Digital Medicines Manufacturing Research Centre (DM²) project and will be further developed through MediForge Platform 4. The MediForge programme team will benefit from onboarding and ongoing training activities during the project. The University partners in MediForge have committed to up to 26 PhD studentships over the 7 years of the programme. Training and development via the Living Lab will benefit the Hub team, the wider stakeholders and the talent pipeline of staff in this sector.

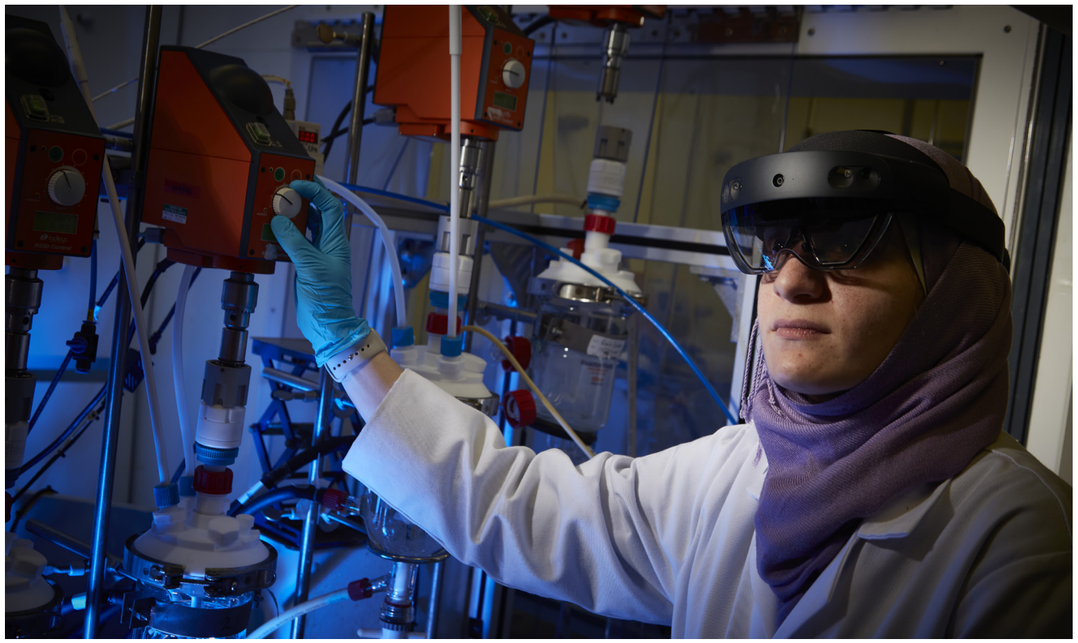


Image: Living Lab with immersive environments

Platform 5: Global Hub

The goal of MediForge is to become a global Hub providing international leadership in the research, development and innovation community. In doing so, it will drive the transformation of Industry 5.0 medicines manufacturing and modernisation of Chemistry, Manufacture and Control (CMC) procedures.

DESIRED OUTPUTS:

- Peer reviewed publications
- Industry 5.0 white papers
- Start multiple industry funded TRL 3-5 projects
- Start new projects for translation of research with third-sector partners
- Co-investment growth
- Spin-outs or significant private capital investments
- XR public engagement packages
- 4 Open Days with >200 participants per event

MediForge is building on CMAC's proven track record to establish itself as a global critical mass research centre, leading the pharmaceutical manufacturing research sector and fostering engagement. MediForge will shape the future of Industry 5.0 medicines manufacturing by advocating for research, training, and translation initiatives, as well as influencing policy, standards, and regulatory modernisation. Our team will inspire and involve the public by sharing the benefits of Industry 5.0, gathering perspectives on emerging technologies, and inspiring future generations of researchers through interactive XR experiences.

Our commitment to knowledge dissemination is reflected in ambitious targets for numbers of high-quality publications, talks, white papers, best practice guides, and impact case studies that will come out of this project.

As a global Hub for collaboration, we will host major events including the CMAC Open Days 2025 (first one is March 18-20, Glasgow, UK), bringing together the Medicines Manufacturing Community. Additionally, we continue to expand our research portfolio, nurturing innovation and ensuring impactful industry translation. MediForge will leverage over a decade of industry-academic partnerships via our User Engagement Strategy that will promote collaboration and seek new opportunities.

Sustainability

Bringing sustainable CMC workflows into real-world industry applications

Resilience

Translation to industry advanced, responsive, model-driven CMC procedures and adaptive processes

Human-Centric Innovation

Developing a diverse, multi-skilled workforce ready to drive Industry 5.0 transformation for medicines manufacturing

Mediforge Partners

Applied Materials · AstraZeneca · Bruker · CCDC advancing structural science · Chiesi · Clairet Scientific Limited · digiM · UKRI Engineering and Physical Sciences Research Council · The Glasgow School of Art · Imperial College London · University of Leeds · Lilly · M-Star · NMIS National Manufacturing Institute Scotland · Pfizer · Roche · sanofi · University of Sheffield · Siemens · University of Strathclyde Glasgow · Takeda · Technobis crystallization systems · UCB · U Lab

Research Portfolio

GI BIO

The Gastrointestinal Bioreactor Facility (GIBio) is the latest addition to the Strathclyde Institute of Pharmacy and Biomedical Science, housing two state-of-the-art engineered models of the gastrointestinal tract.

Oral administration is the most common drug delivery route, reliant on the disintegration and release of the drug in the gut followed by dissolution and absorption into the bloodstream. The complex interactions between the gastrointestinal tract, the dosage form, and the drug determine this process. Using systems developed by the TIM Company, GIBio aims to explore these complex and dynamic interactions.

TIM-1 models the stomach and small intestines, consisting of the duodenum, jejunum, and ileum; TIM-2 models the proximal colon. True-to-life secretions and simulated peristaltic movement within the systems are controlled by protocols that replicate the dynamic environment of the gastrointestinal state. This includes healthy adults, children, paediatrics, and diseased states, allowing GIBio to investigate interindividual variability and promote the need for patient-centric product development.

Output from the TIM systems have been reported as “near clinical” negating the need for animal and human studies at the early stages of product development, working with The University of Strathclyde to promote the 3Rs alternatives to animal studies.

Funded by the EPSRC Strategic Equipment Grant, GIBio aims to provide an early understanding of in vivo product performance to enable the product design and manufacture to be optimised earlier in the development timeline and underpin the data requirement for the BPCS.

GIBio is accepting applications for collaboration from both internal and external parties.

Image: Gastrointestinal Bioreactor Facility

PHARMACRYSTNET: IMPROVING THE PREDICTIVE CAPABILITIES OF CRYSTALLISATION MODELS IN PHARMA

Current methods used for model-based design of crystallisation processes are not always accurate, failing to capture significant and commonly encountered phenomena such as polymorphism, agglomeration or fouling.

Funded under the EPSRC Accelerating the Medicines Revolution call, PharmaCrystNet aims to change that by blending cutting-edge hybrid machine learning and physics-based computing techniques with our understanding of chemistry and chemical processes. Supported by industry partners Pfizer, UCB, Siemens Industry Software Ltd, and CCDC, it aims to:

1) Develop a detailed understanding of the molecular descriptors of drug molecules that dictate crystallisation outcomes.

2) Develop a new hybrid/ML/mechanistic/physics-informed model that can predict crystallisation outcomes under a wide range of industrially relevant process conditions at different scales with high accuracy.

3) Test, refine, and validate the model using real-world experiments from a systematic dataset covering a broad range of molecules and crystallisation behaviours.

Launched in September 2024, PharmaCrystNet will run initially for 12 months to demonstrate the feasibility of the model and approaches developed.

As a part of the process to capture real data for model refinement and validation, solubility curves of more than 120 combinations of solutes and solvents have been gathered so far. Additionally, modelling of neural networks and exploration of molecular descriptors are being explored using simulated data.

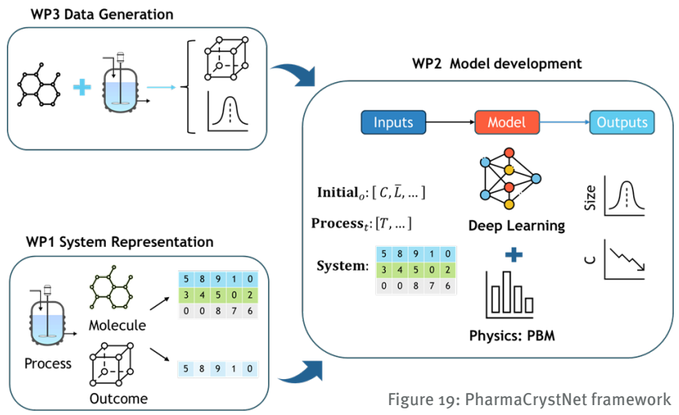


Figure 19: PharmaCrystNet framework

DDMAP

Digital Design and Manufacture of Amorphous Pharmaceuticals

An EPSRC funded project supporting international research collaboration with University of Strathclyde, University of Copenhagen, and Ghent University

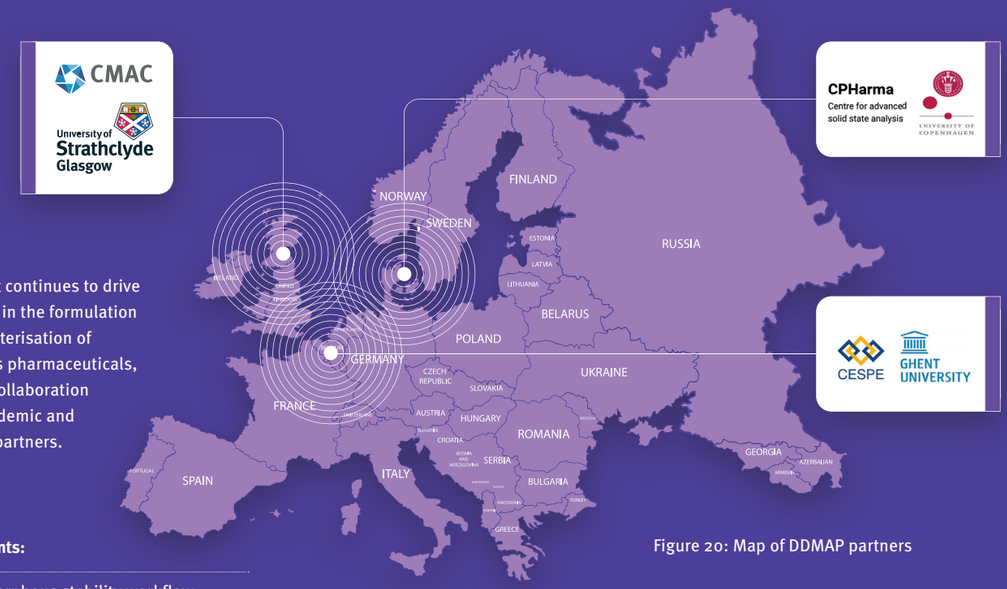


Figure 20: Map of DDMAP partners

The project continues to drive innovation in the formulation and characterisation of amorphous pharmaceuticals, fostering collaboration across academic and industrial partners.

Achievements:

- Amorphous stability workflow implemented
- Initiation of the first round of collaborative projects focused on molecular dynamics simulations, hydrochlorothiazide milling simulations, and imaging techniques for amorphous solid dispersions
- Secured a project extension from EPSRC, with a new end date of 30th April 2026

Collaborations & Knowledge Exchange:

- Visits to Copenhagen and Ghent (Feb & June 2024) for collaboration, and knowledge sharing
- Training at CCDC for software development in amorphous structure analysis (March 2024)
- Collaborative visit by Kensaku Matsunami (Ghent PDRA) to CMAC (May 2024)
- Participation in 2nd AstraZeneca showcase event (July 2024)

Conference Presentations:

- Team members presented at the Royal Society of Chemistry Formulation Science and Technology Event (Feb 2024)
- **Michael Devlin** (WP1) and Daniel Powell (WP3) presented at the PSSRC Symposium, TU Dortmund, Germany
- **Aaron Smith** (WP2) presented his application note at the 2024 European SIFT-MS Symposium, Prague, Czech Republic

Publications:

- **Bordos et al.:** Probing the interplay between drug saturation, processing temperature and microstructure of amorphous solid dispersions with synchrotron X-ray phase contrast tomography (International Journal of Pharmaceutics)
- **Aaron Smith et al.:** Real-time analysis of volatile emissions by coupling SIFT-MS coupled with thermogravimetric analysis (Application Note)
- **J. Axel Zeitler et al.:** Impact of immediate release film coating on the disintegration process of tablets (Journal of Controlled Release)

COMPUTER AIDED SOLVENT DESIGN TO MINIMISE SOLVENT USE IN INTEGRATED SYNTHESIS, PURIFICATION & ISOLATION FOR SUSTAINABLE PHARMACEUTICAL MANUFACTURING (SOLVIT)

SolvIT is a £3.5M, 3-year EPSRC funded project that builds on existing collaborations between Strathclyde and Imperial in the areas of isolation modelling and solvent design, with industrial partner Eli Lilly, to tackle waste in the pharmaceutical industry, and is led by Professor Chris Price (Strathclyde). The objective of this project is to improve efficiency and reduce waste in the manufacture of new and existing medicines, lowering their cost, and making their production more sustainable and environmentally friendly. Manufacturing API can generate around 100kg of hazardous waste per kg of isolated API, most of this waste is solvent. Reducing this will be achieved through three main programmes of work:

- Identification and deployment of sustainable solvents in medicines manufacture: SolvIT will use a combination of computer modelling and experiments to evaluate alternative solvents which are more sustainable in the most popular chemical reactions used in the synthesis of new medicines, so that new and existing process can use these new solvents, reducing waste and cost.
- Integrated solvent and process design: Computational modelling approaches will be combined with process design, driven by a range of key metrics, to allow multiple steps in the medicine production to be combined or “telescoped”, minimising waste that is generated and reducing time to production. Applying lifecycle analysis proactively in this way will result in environmental and financial cost savings.
- Stakeholder engagement: Pharmaceutical company partners and industry regulators will be engaged with to understand challenges current facing solvent recycling and communicate new developments emerging from this work.

Integration of these strands of research, along with the collaborative expertise from the project partners across the disciplines of synthetic chemistry, computational chemistry and chemical engineering, will deliver benefits across the pharmaceutical industry and chemicals manufacturing in general.

Images: Pharmaceutical manufacturing plant

ACCELERATED DISCOVERY AND DEVELOPMENT OF NEW MEDICINES: PROSPERITY PARTNERSHIP FOR A HEALTHIER NATION

This is a collaborative project with GSK as the lead industrial partner. Working with colleagues from the University of Nottingham, CMAC have been working on Theme 4: A new Digital Design toolset to enable Digital Manufacturing of novel pharmaceuticalprocessing equipment.

Theme 4 has focused on leveraging the freedom of design afforded by additive manufacturing (AM) processes to explore non-traditional reactor layouts and the incorporation of additional functionality that would not be possible with traditional equipment. At the request of GSK, the performance of full size production coil flow invertor (CFI) reactors have been investigated. A range of reactor designs have been optimised using computational modelling, prototypes produced using 3D printing technology and their performance evaluated on the project test rig. Data from the evaluation was fed back into the computational modelling to inform the optimisation of the reactor design. As a result, a novel multi-layer reactor has been developed and GSK have been provided with an optimal reactor design for their specific case study which has undergone testing at the Rockville site. To enable GSK to explore other designs, Theme 4 has also created and shared an Excel file that uses the trained machine learning meta-model to predict the residence time distribution of CFI reactors whose parameters fall inside the parameter’s space used during the meta-model’s development.

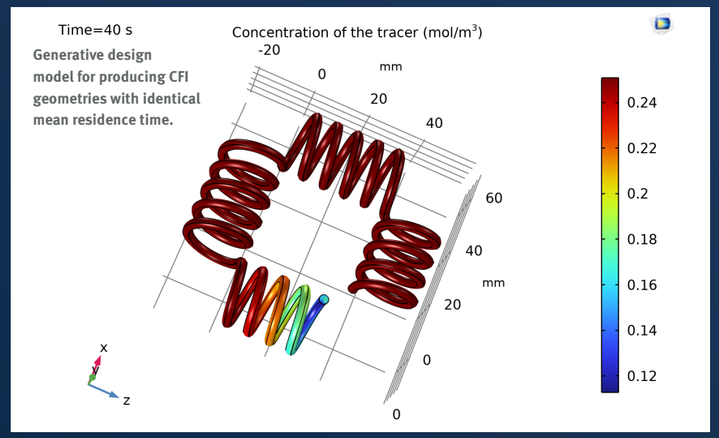


Figure 21: Novel reactor

DIALLING UP PERFORMANCE FOR ON DEMAND MANUFACTURING (3DP)

3DP is a £5.8M, 5-year EPSRC funded collaboration between the Universities of Nottingham, Reading, Cambridge and Strathclyde, along with a range of industrial and innovation partners including Pfizer, AZ, GSK, and CPI. The aim is to give the tools to industry that they need to adopt 3D printing – developing a toolkit that automates and smooths the path from concept to realisation.

The development of this toolkit will be driven by three challenging product demonstrators – a pill for biologics, a patch for intestinal regeneration and a reactor for enzyme catalysis. The team will use these paradigm changing products to combine high throughput screening, automation and machine learning into workflows and tools that industry will use to create highly functional, smart 3D printed products with the potential to transform key UK industries - (bio)pharma, cell therapy and regenerative medicine and (bio)catalysis and beyond.

Over the past 12 months, research at Strathclyde has focused on establishing data systems to capture the rich scientific data being generated across the project as well as the data science tools required to analyse these complex data sets.

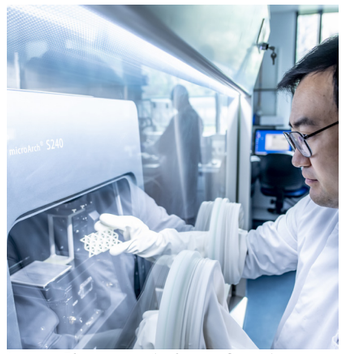


Image: Pharmaceutical manufacturing

RIFTMAP

Right First Time Manufacturing of Pharmaceuticals (RiFTMaP) was a three-year, £2 million project funded by the EPSRC and US National Science Fund (NSF). This project was a collaboration between the University of Sheffield, University College London, the University of Strathclyde, and Purdue University and it was supported by industrial partners from across the pharmaceutical, software, and equipment manufacturing fields: Alexanderwerk, AstraZeneca, Eli Lilly, GlaxoSmithKline, Pfizer, IBM UK, Lannett, Napoli Scientific, and Process Systems Enterprises.

RiFTMaP focuses the development of smart manufacturing systems to enable “right first time” (RFT) manufacturing, which incorporates Industry 4.0 concepts as part of a systematic framework for continuous manufacturing of pharmaceuticals, with the goal of delivering systematic benefits to the pharmaceutical industry, such as:

- Reducing the time to market for new products
- Minimising waste during manufacturing and development
- Improving the resilience and robustness of manufacturing lines
- Reducing the costs of development and manufacturing

This project aims to deliver a framework and computational tools for the optimal design of pharmaceutical processes, with a real-time process management system and a flexible real-time release testing framework. All models, controls and optimisation procedures are validated at pilot scale, using three cutting edge manufacturing lines: the Consigma 25 wet granulation line at the University of Sheffield; the dry granulation line at Purdue University; and the continuous direct compression line, also at Purdue University.

The first annual technical meeting was hosted by the University of Sheffield in June 2022. This provided a platform for the academic partners to provide updates on each work package and to discuss the direction of further development and collaboration with industry perspective. The next technical meeting was hosted by Purdue University in June 2023, with the next meeting hosted by CMAC in Glasgow in 2024. The University of Strathclyde team have developed a flexible model for the in vitro dissolution performance of directly compressed products, using only raw material characteristics as inputs. This model was developed to be used to implement real-time release testing in the direct compression line, and will be further developed to suit the granulation lines.

Image: Consigma 25 at Sheffield

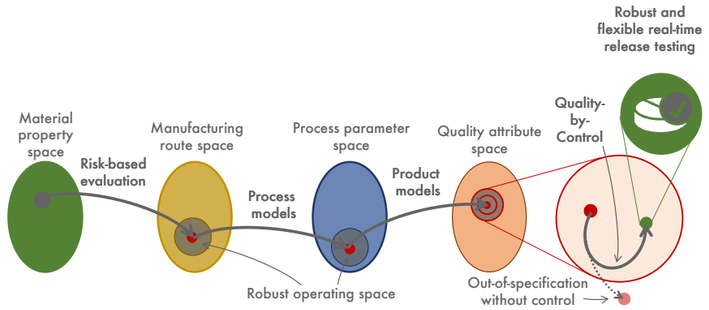


Figure 22: RiFTMap framework

MADE SMARTER INNOVATION

DM² Digital Medicines Manufacturing

The Digital Manufacturing Research Centre (DM²) is revolutionising the field of medicines manufacturing through the implementation of integrated industrial digital technologies (IDTs).

This 3.5-year project aims to minimise waste, enhance efficiency, and cultivate a future-ready workforce to improve the agility of the medicines manufacturing sector.

By achieving these goals, DM² is contributing to the faster and more sustainable delivery of medicines to patients.

2024 highlights

Tableting DataFactory

The DM² Tableting DataFactory accelerates tablet formulation and process development to under 24 hours, using only a few grams of material. The AI-driven robotic platform, coupled with predictive system of models, rapidly selects and optimises formulation and process conditions, ensuring they are ready for scale-up.

SkillsFactory

Filling a void in the digital skills gap, this new online platform is set to deliver industry-aligned courses to ensure up to date knowledge in the pharmaceutical sector. It is now being used by CMAC students offering flexible learning and is set to be launched externally in 2025.

Extended realities (XR) in medicines manufacturing

XR has transformed the opportunities for medicines manufacturing. Using augmented reality (AR), the team has been visualising data enabling data-driven decision making.

Using mixed reality (MR), the team has facilitated real-time, structured remote monitoring.

This has enhanced training, safety and virtual collaboration, helping to boost productivity and efficiency.

3.5 years to deliver project objectives

£5m co -founded by the Made Smarter Innovation challenge at UK Research & Innovation

32 Industry partners co-investing and co-creating

Research outputs and engagement 2024

24 demonstrators developed across five research platforms using **7** industrial digital technologies (IDTs)

7 IDTs developed: data collation & transformation, machine learning/AI, computer modelling, robotics, digital design, and, immersive tech

24 Events reaching thousands of stakeholders

28 Papers published. – 13 released in 2024

Delivered **53** external research presentations

>£2.5M Co-investment in DM² projects

2 Use cases completed

Acted as contributor to **£2.75m** funding bids

54 PhD researchers trained at CMAC Summer School

Business plan approved to launch **CMAC SkillsFactory** in 2025

614 Workers upskilled in the use of digital technologies






SHARPEN (SHARING DATA TO ACCELERATE PHARMACEUTICAL MANUFACTURING EFFICIENCY ACROSS TRUSTED NETWORKS)

The SHARPEN project aims to transform pharmaceutical manufacturing by addressing the data-sharing and intellectual property (IP) challenges that limit the application of advanced modelling techniques. By leveraging federated learning (FL) technologies, SHARPEN seeks to enable efficient, secure, and trusted data sharing across manufacturing and R&D environments.

The project will develop a framework demonstrating that data sharing improves predictive modelling accuracy and manufacturing efficiency. Key innovations include a risk assessment tool for secure data sharing, ensuring intellectual property protection and addressing concerns about commercial risks, as well as the federated learning platform itself. These efforts will support the creation of well-validated machine learning models derived from diverse datasets, advancing the industry's digital and data-driven capabilities.

SHARPEN's outcomes offer significant impacts: improving manufacturing efficiency, reducing waste, and fostering collaboration between and across academia and industry. The project aligns with initiatives across the CMAC portfolio, advancing the UK's leadership in digital pharmaceutical manufacturing and setting a precedent for secure, collaborative innovation in the sector.

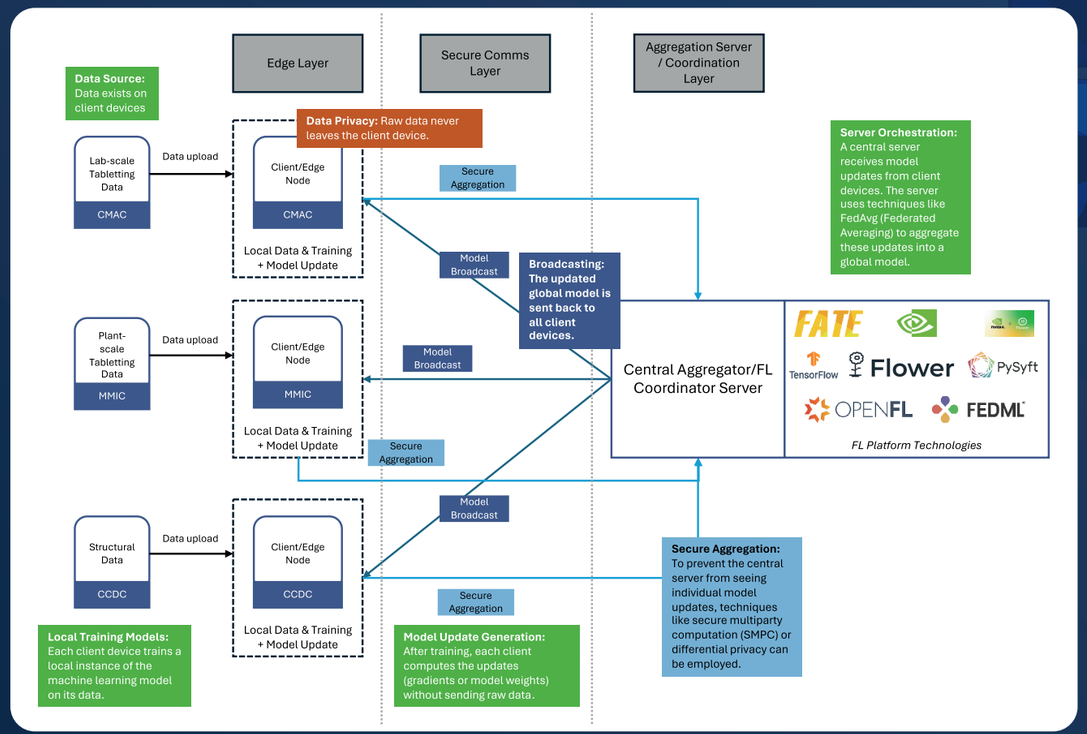


Figure 23: Federated Learning technologies offer a means to share data securely without compromising sensitive IP. The architecture and examples of leading FL technologies to be assessed are shown below.

INNOVATE UK KTP WITH ASTRAZENECA: ROUTINE EXPLOITATION OF PAIR DISTRIBUTION FUNCTION IN PHARMACEUTICAL DEVELOPMENT

The Knowledge Transfer Partnership (KTP) between CMAC at the University of Strathclyde and AstraZeneca (AZ) has successfully enhanced AZ's capabilities for exploiting amorphous and low-ordered materials. These materials are becoming increasingly significant in pharmaceutical pipelines due to the rising complexity of active pharmaceutical ingredients (APIs).

The project introduced advanced structural characterisation techniques, such as Pair Distribution Function (PDF) analysis and structural modelling, into AZ's workflows, establishing them as routine practices.

From a CMAC perspective, the collaboration enabled the translation of academic expertise into industrial applications, reinforcing the Centre's commitment to advancing pharmaceutical manufacturing through data-driven innovation.

The project provided AZ with tools to better manage batch-to-batch variability, optimise solid form control strategies, and improve product performance. These advancements align with AZ's strategic objectives of accelerating time-to-market and enhancing sustainability by reducing material waste and batch failures.

This KTP has benefited AZ, by equipping them to address the challenges associated with amorphous materials while positioning CMAC as a pivotal partner in shaping the future of pharmaceutical development. The tools and methodologies developed, including experimental protocols and workflows for structural modelling, are now embedded in AZ's practices, fostering long-term improvements in efficiency and product quality.

This collaboration exemplifies the value of academia-industry partnerships in driving impactful innovation for the pharmaceutical sector.

COMMUNITY FOR ANALYTICAL MEASUREMENT SCIENCE (CAMS) INDUSTRY PROJECT: PHYSICAL STABILITY CHARACTERISATION AND PREDICTION

This collaborative project between CMAC, AstraZeneca and Pfizer aims to gain a deep understanding of the relationship between material attributes, the temporal nano- and microstructural evolution of pharmaceutical tablets and their impact on in-vitro drug release performance after long-term storage.

Using CMAC's cutting-edge technologies such as X-ray computed nanotomography, terahertz time-domain spectroscopy and optical coherence tomography, the project team visualises and quantifies structural changes of pharmaceutical tablets across length-scales ranging from nanometers to millimeters.

The research involves the collaborative efforts of three PhD students and one post-doctoral researcher, each dedicated to the investigation of raw and compacted materials at various process parameters subjected to accelerated stability conditions. The primary focus is the characterisation of these materials, advancing our understanding of the interplay between raw material characteristics and product physical stability.

A key accomplishment from the project to date is the development of a single-particle model describing the swelling behaviour of excipients. The model solely relies on input parameters obtained from dynamic vapor sorption (DVS) data, allowing an accurate prediction of the swelling and moisture uptake of powder. Validation of the model involved comparison of model predictions against experimental particle size data. The investigation further includes the analysis of X-ray computed tomography data for compacted samples subjected to accelerated stability conditions. The use of X-ray CT data is pivotal for assessing structural changes in samples subjected to accelerated stability conditions, thus contributing to the development of a stability model that captures the underlying mechanisms.

The project delivers workflows and innovative digital tools that can predict long-term changes in drug release kinetics, thus contributing significantly to CMAC's strategic goals of delivering digitally enabled R&D with benefits such as accelerating medicines development, reducing cost, and improving environmental impact.

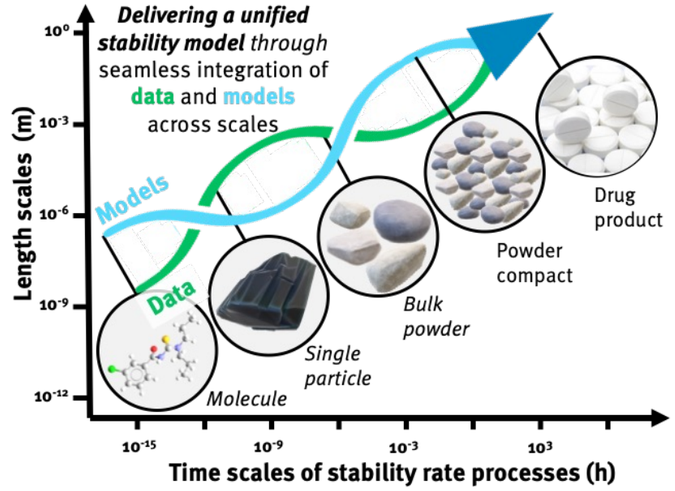


Figure 24: Understanding the relationship between material attributes, temporal nano- and microstructural evolution, and in-vitro drug release performance of pharmaceutical tablets after long-term storage

DPN-MED: DIGITAL PLUG AND PLAY NETWORK FOR SUSTAINABLE MEDICINES DEVELOPMENT AND MANUFACTURING

THE GRAND CHALLENGE EOI PHASE

Pharmaceutical emissions are 55% higher than those of the automotive industry generating up to 100kg of waste per kg of product. This carbon footprint is expected to increase further due to the rise in smaller production volumes, personalized therapies, and increasing complexity of molecules and processes.

This Grand Challenge project aims to transform how medicines are made by shifting from outdated, costly medicine development and manufacturing systems to automated and resource efficient approaches. This new approach will integrate advanced digital tools with Medicines development and manufacturing technologies, allowing labs and factories to produce medicines more efficiently and with less waste. A key feature is the creation of a network of self-driving development and manufacturing systems, which can communicate, operate and share information securely in real-time.

DPN-MED drives sustainable medicines manufacturing by reducing emissions, waste, and energy use while boosting productivity and creating jobs. It accelerates drug development, enables personalised treatments, and enhances security of medicines supply. Key impacts include cutting raw material use, clinical trial stock waste, and establishing global greenhouse gas standards, fostering economic, societal and environmental advancements.

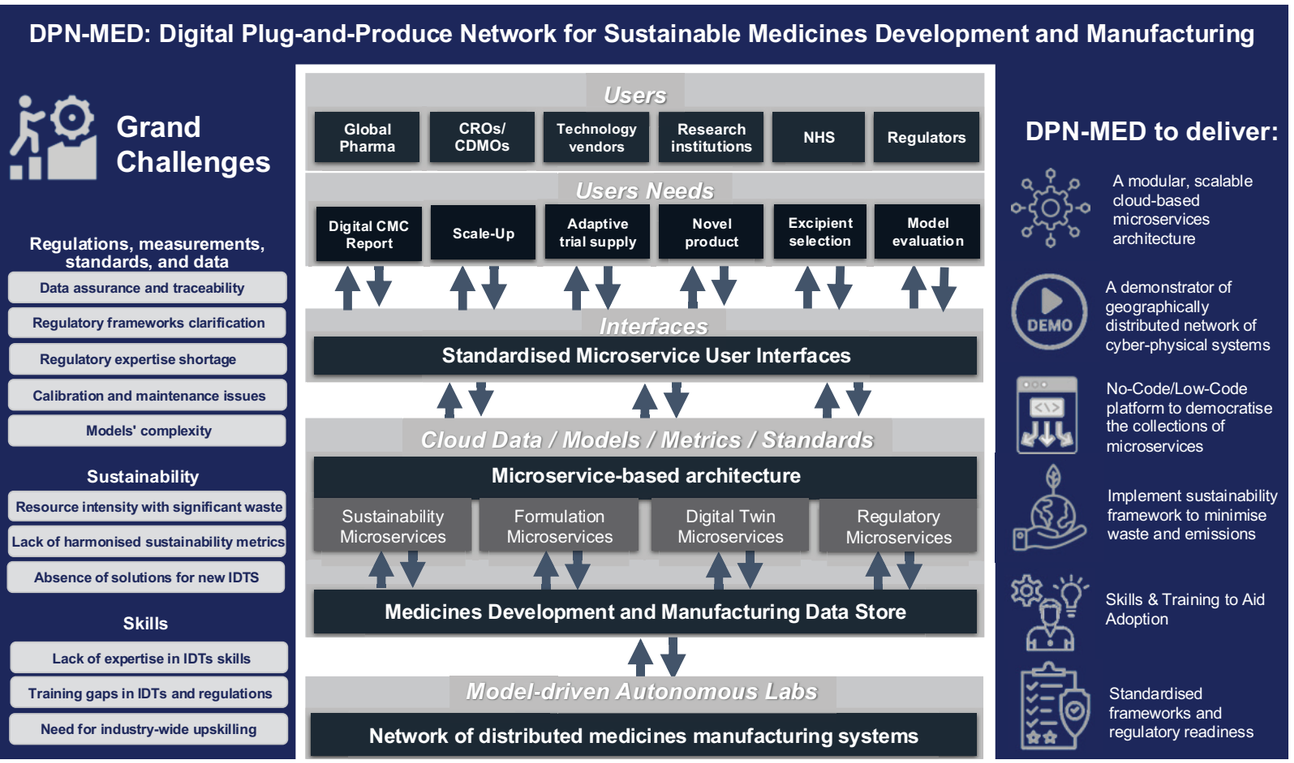


Figure 25: Summary of DPN-MED Grand Challenge

CERSI: A REGULATORY SCIENCE NETWORK FOR THE DIGITAL TRANSFORMATION OF MEDICINES DEVELOPMENT AND MANUFACTURING

A 6 month programme was carried out by CMAC, AZ, BMS CCDC, and Siemens to build a consortium and develop a fuller detailed proposal to submit a full bid for a UK Centre for Regulatory Science and Innovation (CERSI) funded by UK MHRA and Innovate UK. The team, carried out workshops and meetings with MHRA and interested parties, plus questionnaires to develop the following:

Vision: This Centre of Excellence in Regulatory Science and Innovation (CERSI) in medicines development and manufacturing aims to unlock the benefits of the digital transformation of Chemistry, Manufacturing, and Control (CMC) for the pharmaceutical industry, regulators and the broader society.

Objectives

- Establish a sustainable and influential CERSI that generates impact for patients, the planet and the UK economy and address regulatory challenges, focusing on regulatory science and innovation in:
  - 1) AI and predictive models (e.g. crystal structure)
  - 2) autonomous data generation (e.g. robotics) including data systems (e.g. ontologies)
- Demonstrate leadership in global regulatory engagement to advocate and influence policies for digital technologies in CMC
- Establish a forward-looking standardised regulatory framework to enhance confidence in digital tools, breaking down siloed efforts and ensure regulatory maturity, demonstrated through impactful use cases
- Create scalable and impactful training programmes focusing on digital CMC regulatory science and innovation

With new project partners De Montfort University, GSK and Pfizer joining during the EoI, the team were successful in the full application and the full 1-year funded project starting on 1st February 2025.

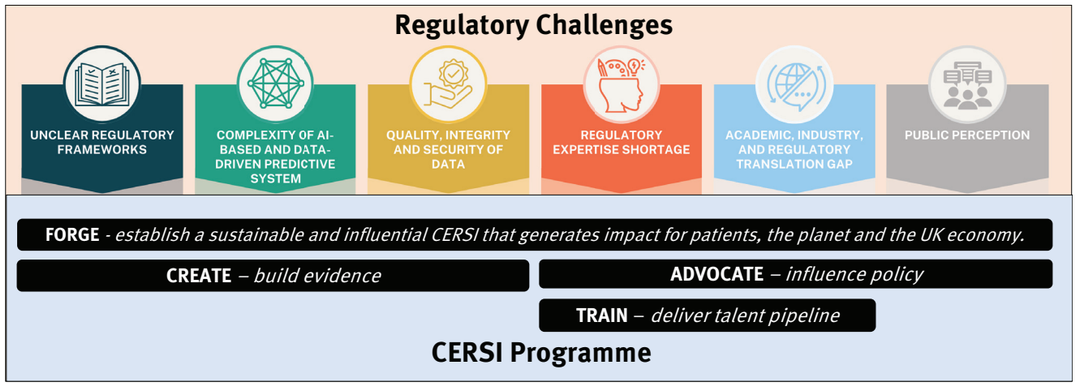


Figure 26: Summary of CERSI Network

MMIC GRAND CHALLENGE 1: TRANSFORMING TABLET PRODUCTION

The Medicines Manufacturing Innovation Centre is a collaboration between the Centre of Process Innovation (CPI), University of Strathclyde, UK Research & Innovation, Scottish Enterprise and founding industry partners, AstraZeneca and GSK.

For Grand Challenge 1, the Medicines Manufacturing Innovation Centre collaborated with technology experts CMAC alongside AstraZeneca, GSK, Pfizer (pharmaceutical partners); Gericke (equipment partners); DFE Pharma (excipient partners); Applied Materials and Siemens (software and digital solution partners) to develop a digitally twinned Continuous Direct Compression (CDC) platform and equipment workflow.

The project was selected by the Medicines Manufacturing Innovation Centre founding partners as the first Grand Challenge to accelerate the adoption of novel CDC technology into a higher technology readiness level (TRL). The project will support the industry to shift from traditional large batch manufacturing approaches, to one that is continuous using either continuous blending or a miniblend approach. Adoption of this technology across the wider network would ultimately increase understanding and acceptance to utilise this new technology. Coupled with the predictive Digital Twin, this fully flexible, modular and vendor agnostic CDC line can then be used as a demonstrator for oral solid dose process development.

Transforming the way industry makes tablets, combining continuous manufacturing direct compression methods with digital prediction capabilities. As continuous manufacturing is built around a steady state operation, it provides multiple benefits to industry:

- Reduces the amount of starting materials needed for process development, both physically and digitally by using the Digital Twin to optimise the process in silico
- Reduces the cycle time of manufacture
- Decreases the carbon footprint of manufacture
- Reduces the overall cost of the technology for the end-user

This project forms part of the translation to industry framework, accelerating translation of innovative technologies into practise.

Within CMAC, a dedicated team successfully managed the complex technical aspects of the project. The team led by Associate Director Professor John Robertson collaborated both within the University of Strathclyde's facilities, and then subsequently at the Medicines Manufacturing Innovation Centre after installation and commissioning of the line from 2023. The test bed was designed and built by CMAC and transferred to MMIC with ongoing technical development and support. Critical aspects undertaken were:

- Deep characterisation of the constituent unit operations (Feeders, Blenders, Tablet press)
- PAT interface development and its impact upon residence time distribution
- Modelling of associated unit operations (blender macromixing Residence Time Distribution (RTD) / micromixing Relative Standard Deviation (RSD) / Extent of lubrication, Feedfactor performance and variability, Feed frame macromixing RTD and compaction
- Full line modelling flow sheet verification

Alongside the Operations team at the Medicines Manufacturing Innovation Centre, CMAC has successfully trialled and verified the CDC line against the Digital twin model prediction. These tests the led the way for process development on proprietary partner compounds utilising the Digital Twin and model infrastucture to expedite process optimisation and understanding.

The project development phase completed in March 2024 and the CMAC team have subsequently generated a series of 6 publications covering the model and sytem development activities.

Image: Feeder units

Image: Full CDC line located at MMIC

WATCH THIS SPACE:

- Containment installation to permit development on potent material to OEB_4 level
- Journal Publications of Grand Challenge 1 outcomes
- Capbility now available for customer projects
- Development of new collaborative projects exploring beyond Grand Challenge 1

Industry Funded Core Projects

The Pre-Competitive Core Projects are funded collectively by CMAC's Tier 1 partners and are designed to develop translatable outputs to deliver impact in research areas.

Industrialisation of Spherical Agglomeration

University of Strathclyde, 1 year project (2x PDRA FTE), started April 2024

The aim of this project is to build understanding around the feasibility of scale up of spherical agglomeration processes through both modelling and experimental workflow development, to robustly deliver consistent and size controlled spherical agglomerates for downstream processing.

ACTIVITIES:

- Decoupled kinetic study to develop:
  - 1) fundamental process & mechanistic understanding
  - 2) parameterising sub-models for multi-step agglomeration design
- Agglomeration scale-up feasibility study to evaluate the effects of process conditions (such as solid loading, shear conditions and bridging liquids-to-solids ratio) on product attributes and isolation performance
- Establishing and validating scaling rules across 1L, 5L and 25L scales for two bridging liquid systems
- Workflow for agglomerate strength characterisation & modelling
- Multivariate-informed Design of Experiments to enhance agglomerate tuneability, support population balance model development and inform scaling guidelines across multiple systems

OUTPUTS:

- Process and mechanistic understanding including know-how for scale-up of spherical agglomeration and isolation up to the 25L scale
- Identified, monitored and modelled agglomerate coalescence-driven growth phenomena based on experimental evidence for improved predictive capabilities.

Automated Model Based Design of Experiments for Crystallisation Process Development

University of Strathclyde, 1-year project, started early 2024

The aim of this project is to develop a model-based Design of Experiments workflow that can be executed on an automated crystallisation platform. The objective of such a workflow would be the optimisation towards target process parameters via the generation of a process model with an acceptable uncertainty.

ACTIVITIES:

- Undertake a literature review on recent developments of automated chemistry, particularly in pharmaceutical research
- Demonstrate the capability of an 'off the shelf' automated crystallisation platform for the execution of a predefined list of experiments
- Develop a model-based Design of Experiments approach that takes data from an initial set of experiments and proposes the most optimum experiment to perform to achieve the objective
- Demonstrate capability of the automated crystallisation platform to execute the model-based Design of Experiments experiments and repeat until target process parameter objectives are achieved

OUTPUTS:

- Detailed literature review of optimisation and predictive modelling tools for Design of Experiments for crystallisation processes
- Workflow for running the automated DoE utilising algorithms for the optimisation of crystallisation processes for yield and particle size
- Comparisons between different modelling approaches for optimisation of crystallisation processes including population balance, data-driven and a hybrid approach

Exemplary Translation to Industry

As CMAC accelerates its transition toward a global dynamic industry portfolio, we continue to strengthen our research and innovation agenda, ensuring our impact is tangible and transformative. With a thriving portfolio of digital chemistry, manufacturing, and controls (CMC) solutions, patents and an increasing number of strategic initiatives materialising into real-world use cases and end-to-end test beds, CMAC is at the forefront of advancing industrial application in pharmaceutical advanced manufacturing.

Our commitment to industry leadership is reflected in the continued evolution of our research portfolio, particularly in the accelerated deployment of our CMAC DataFactories and key research streams: CCS, MCS+, BPCS, and Quality by Digital Design (QbDD). These initiatives drive the transformation of medicines manufacturing at an industrial scale, enhancing efficiency, sustainability, and patient access to affordable manufacturing and to high-quality therapies.

By integrating industry-driven strategic intents with cutting-edge research, CMAC is building an ecosystem where collaborative ideation, co-creation, and co-delivery create direct pathways for technology adoption. This transition strengthens our role in accelerating the UK's advanced manufacturing roadmap while also delivering a global impact.

CMAC provides multiple pathways for industrial translation, including staff exchanges, company placements, industry workshops, expert training programs, and e-learning modules. Additionally, our pre-competitive industry-funded programs serve as catalysts for strategic partnerships, enabling seamless technology transfer. A prime example is our ongoing collaboration with CPI, leading CDMOs, and specialty pharma, bridging academic innovation with industrial-scale implementation.

Our research strategy roadmap aligns with the evolving needs of industry, regulators and emerging scientific knowledge, particularly focusing on the digital transformation of CMC. This vision redefines pharmaceutical manufacturing, embedding sustainability, agility, and a patient-centric approach into future supply chains.

With over a decade of leadership as an international Centre for Future Manufacturing Research, Translation to Industry and Training, CMAC has solidified its position as a global hub for industrial, academic, and innovation-driven collaborations. Our proactive engagement with industry stakeholders, government agencies, and global research communities ensures that we remain at the cutting edge of pharmaceutical manufacturing—translating groundbreaking research into industrial impact that benefits both companies and patients worldwide

Massimo Bresciani,
CMAC Industry Director

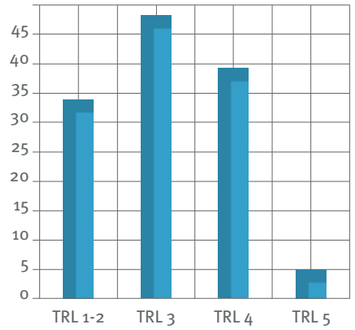
Overview

CMAC's world-leading research programme and exemplary translation to industry (T2I) strategy is informed and co-created through close collaboration with industrial partners to deliver tangible benefits and impact. Our technical portfolio has seen a huge increase to 126 technologies that are now translatable to industry. These assets include knowhow and expertise, through to equipment, workflows, individual models, apps, and AI models building on to large data across a range of Technology Readiness Levels (TRLs).

Our aim is to enable the digitalisation of Chemistry, Manufacturing and Control (CMC) processes and establish Cyberphysical Systems (CPS) for medicines development and production processes through our platform technology areas. This will be achieved through the development of technologies in line with the Quality by Digital Design framework (QbDD), that will integrate the three novel integrated Classification Systems outlined in the CMAC strategy document; the Crystallisation Classification System (CCS), Manufacturing Classification System (MCS+), and Biorelevant Performance Classification System (BPCS).

CMAC's translation to industry programme of activities supports multiple routes to translation concentrating on the digitalisation of CMC to support the integration of QbDD into industrial applications. These provide excellent opportunities for companies in the UK and internationally, both large and small, whether technology provider or large-scale pharmaceutical manufacturer to work with CMAC and help accelerate the adoption of advanced pharmaceutical manufacturing.

TRL based development and progression	T2I via strategic partnerships T2I in collaboration with Tier 1, Translation to Industry Collaborators or Tier 2 partners
Staff Exchanges	PhD placements at companies Company Staff at CMAC
PhD at Work	Undertake PhD whilst continuing to work
Recruitment	Access to CMAC talent pipeline
Collaboration	Engage in pre-competitive industry-funded programmes Network across industrial partners and attend CMAC events
Facilities and expertise	Carry out 1:1 proprietary projects using CMAC world class facilities and dedicated team of experts Use CMAC as a test bed for equipment and processes, de-risking internally
Staff training	Webinars and e-learning platform Staff CPD at CMAC/site



Innovative Technology Portfolio

Technology assets have increased from **23** in **2019** to **126** in **2024**

CMAC's innovative Drug Product DataFactory undergoing commercial readiness planning for full-scale industrial implementation

Commercial Microfeeder under development towards commercial readiness

CMAC enabled crystallisation optimisation system undergoing validation

Figure 27: Technology portfolio assets

2024 Summary

In 2024, CMAC continued its strategic expansion and reinforced collaborations with eight global pharmaceutical partners, and welcoming new Translation to Industry collaborators (see page 66). This category of partnership enhances opportunities to translate on an industrial scale with a commercial focus.

By fostering a strategic, dynamic, and engaged ecosystem, CMAC promotes pre-competitive collaboration and drives process improvements across the industry. The impact of these efforts is exemplified by the successful technical translation of key innovations, including the Small-Scale Nucleator Platform, the Multi-Dimensional Particle Characterisation App, and the Cooling Crystallisation Workflow e-learning course.

CMAC's commitment to delivering value to its partners is evident in the effective translation of groundbreaking solutions into practical industry applications. This approach accelerates the advancement of technologies to higher Technology Readiness Levels (TRL), expedites commercialisation, and strengthens industrial applications, remaining a cornerstone of the CMAC Strategy.

Industry Engagement & Translation

CMAC has continued to deliver value to partners through its industry engagement strategy. This is achieved by emphasising the benefits and opportunities attainable through co-creation, co-delivery, dissemination, training and discovery of translation routes to key stakeholders.

Industrial support has been key in the development of the CMAC strategy and their invaluable input into the CCS, MCS+ and BPCS themes has helped sculpt the research programme to ensure translatable assets are of industrial value.

The diverse and rich CMAC technology portfolio has grown through the creation of new technologies at TRL 1-3 and the development of technologies at TRL 3-6, to meet the challenges and emerging needs of industry. CMAC has implemented a stage-gate process for managing these technologies from low to high TRL with input from research teams and Tier 1 end users.

> "We are thrilled to join the CMAC-consortium, as CMAC is a world-renowned centre for crystallisation and formulation studies, and an innovator in the field of digitalisation. Our collaboration may help CMAC in developing solutions for commercial manufacture while we as a company aim to expand our knowledge and expertise in these domains."
>
> Geert Schelkens, R&D Manager Early Phase API and Technology Development at Ajinomoto Bio-Pharma Services

There has also been the organisation of a Translation Committee involving industrial partners to help identify key technologies for development to increase impact and industrial adoption of the technologies across CMAC's strategic themes.

DIGITAL TRANSLATION: CMAC ASSETSTORE

Making our toolbox of digital assets available to internal users to test and apply

To support the growth of the CMAC digital technologies (including workflows, models, databases, datasets and training material) the CMAC AssetStore has been launched. The CMAC AssetStore is a content management system created to accelerate the developed of collaborative digital technologies and prepare the digital technologies for translation.

Figure 28: CMAC AssetStore

TRANSLATING FOR IMPACT:

Multi-dimensional Particle Characterisation App (MDPC)

Through the industry funded core project funding an App that uses Deep learning and machine learning models to predict particle size distributions of crystallisation processes from in-situ imaging (PVM, crystalline etc.) has been developed. The models use a combination of CMAC generated and Tier 1 data to expand the training datasets for the App. This large training dataset allows the model accuracy to significantly exceed the commercial software available in current crystallisation hardware and microscopy probes and meets or exceeds alternative PSD prediction models. The AI enhanced model has been translated to Tier 1 partners for testing on industrial systems.

Key Outputs:

- Revised App with 2 different workflows, updated user manual and 4 test datasets
- 3 Translation workshops at US based Tier 1 partners
- 3 Conference contributions and 2 papers in draft form
- 2 User groups on Teams for CMAC and Tier 1 partners

Bulk powder properties prediction App

Through the industry funded core project funding an App that uses Deep Learning and Machine Learning (ML) models to predict particle bulk properties such as Hausner ratio (HR), Bulk density (BD) and Flow Function Coefficient (FFC) from images (Morphologi G3, Microscopy,) has been developed. The App has two methodologies: the first ML model uses training datasets of HR, BD, FFC and Morphologi text files to build a predictive 2-layer neural network that can allow the prediction of the powder's bulk properties; and the second DL model uses training data of Morphologi frame images and powders HR to build and convoluted neural network to predict HR. The App has been designed to be user-friendly and allow non-expert users to input their data and gain good predictions for their materials of interest. The AI enhanced model has been translated to Tier 1 partners for testing on industrial systems.

Key Outputs:

- App with two different predictive functions and user manual
- 3 Translation workshops at Tier 1 partners
- 1 recorded webinar with over 60 industry attendees
- Technical report

CMAC Tier 1 Partners

CMAC has continued to work in close partnership with our industry partners over the past 12 months, the highlight being able to welcome Sanofi as a new Tier 1 partner. We have jointly worked to execute the CMAC Strategy 2021-2026; we have an excellent portfolio of precompetitive collaborative research, translation and skills projects in the pipeline to deliver value across the international medicines manufacturing landscape.

Tier 1 Membership Benefits

- Peer-to-peer knowledge sharing through the Technical Committee
- PhD placements within industry to advance precompetitive opportunities & skills development
- Collaborative Core Projects with outputs translated to industry needs
- Exclusive member networking events
- Proprietary confidential projects or collaboration models executed within world class facilities at our Glasgow laboratories
- Recruitment of CMAC trained researchers aligned to current and future sector needs access to funding opportunities

Translation to Industry Collaborators

Strengthening Industry Collaboration for Advanced CMC Development

Lonza and Ajinomoto Bio-Pharma Services, two leading Global Contract Development and Manufacturing Organisations (CDMOs), have joined CMAC as Translation to Industry (T2I) Collaborators. This strategic partnership accelerates the digital transformation of CMC by leveraging CDMO expertise in crystallisation, PAT, continuous manufacturing, and digitisation. It strengthens CMAC's translation capabilities, benefits Tier 1 partners, and supports the development of advanced CMC technologies. Marking a key milestone in expanding industry engagement, the initiative will drive adoption of modern manufacturing approaches and create broad impact across the pharmaceutical and healthcare sectors.

CMAC has also welcomed CCDC, Gericke, and digiM as T2I Collaborators within the technology vendor stream. Their strategic alignment and investment will enable clients to execute projects more efficiently, utilising CMAC's expertise and facilities alongside cutting-edge vendor technologies—offering a unique, integrated service solution.

This growing network of industry partnerships reinforces CMAC's commitment to accelerating innovation and transforming pharmaceutical manufacturing through strategic collaborations.

CMAC Tier 2 Partners

CMAC's vibrant Tier 2 community consists of 11 members spanning digital solution/ data analytics, advanced analytical & manufacturing platform providers, consulting firms and specialised contract research organisations. The formal partnership between CMAC and each respective Tier 2 aligns with mutual and strategic objectives.

2024 Highlights:

- Clairet Scientific: Joint publication https://doi.org/10.1039/d4cc05591h
- Element/Syft: 2024 EU SIFT-MS Symposium, Prague, contributions via Prof. Chris Price and Aaron Smith
- digiM: Joint case studies and development of integrated service offerings
- Laminar/Analytik: Characterisation case study and publication.

Industry Engagement with the CMAC Researcher Community

PHD PLACEMENTS WITH CMAC PARTNERS IN 2023-2024

PhD Placements continue to be a crucial part of the PhD research journey. They are a vital link between academic research and its practical applications promoting collaboration and allowing for research to be showcased industrial environments.

CMAC students enjoy participating in industrial placements as they provide the opportunity to implement their knowledge in a professional setting, equipping them with skills that boost their employability.

Irene Moreno Flores, Chiesi, Italy June 2024 - Dec 2024

Project Title: Modelling of a cystallisation process on different size reactors using PBM to predict particle size distribution.

"Seeing first-hand that all the skills I have developed throughout my PhD in CMAC are directly applicable to industry, and how they make a positive impact in the day-to-day operations of a company. In short, an unforgettable experience"

Company	Location	PhD Student	Project Title
AstraZeneca	Remote + Macclesfield, UK	Isra' Ibrahim	Understanding Long-term Physical Stability of Oral Pharmaceutical Dosage Forms
AstraZeneca	Macclesfield, UK	Oliver Towns	Applying a population balance model to optimize a wet milling process for an AZ development project
AstraZeneca	Macclesfield, UK	Suruthi Gnanenthiran	Understanding and predicting the influence of scale-up and dryer geometry on agglomeration behaviour in agitated dryers
Chiesi	Parma, Italy	Irene Moreno Flores	Modelling of a crystallisation process on different size reactors using PBM to predict particle size distribution
GSK	Stevenage, UK	Christopher McArdle	Bisulfite Addition Reactive Crystallisation using a Continuous Flow Setup
Lilly	Indianapolis, USA	Patrycja Bartkowiak	Evaluating the use of external lubrication in tabletting
Sanofi	Remote	Thomas Ralph	Evaluating the application of PINNs in predicting flow physics in a stirred tank
UCB	Brussels, Belgium	Saadia Tanveer	Investigation of Stability and Disproportionation Behaviour of Salt Hydrates with Water Bridge Motif

Saadia Tanveer, UCB, Belgium Sept 2024 – Dec 2024

Project Title: Investigation of stability and disproportionation behaviour of salt hydrates with water bridge motif

"The highlight of my placement was applying the workflow I developed during my PhD to UCB synthesised molecules. Collaborating with experienced scientists and contributing to their ongoing research gave me a sense of accomplishment and purpose. This placement has been an invaluable experience, and it was rewarding to hear the industry team discuss how they could adapt my workflow ideas to determine the stability of their compound."

Outstanding Skills Development

The CMAC community is a thriving place for multi-skilled researchers, driving innovation in medicines development and manufacturing. Our tailored training programmes, shaped by academic experts and industry leaders, utilise CMAC's state-of-the-art facilities, and strong partnerships with global industry leaders to deliver excellence.

Our MSc in Advanced Pharmaceutical Manufacturing and CMAC PhD programmes offer a unique journey for researchers, enhancing both technical and transferable skills, fostering innovation, and building strong professional networks. Early Careers Researchers receive comprehensive training in essential technical and transferable skills, actively engaging with the industry through visits, events and research projects driven by industry needs.

CMAC has solidified a top talent pipeline in advanced pharmaceutical manufacturing. In 2024, five industrial placements took place, 18 new students commenced their studies and five graduated during the year.

Prof Daniel Markl,
CMAC Associate Director

Dr Catriona Clark,
Skills Development Lead

CMAC'S COMPREHENSIVE TRAINING SPANS:

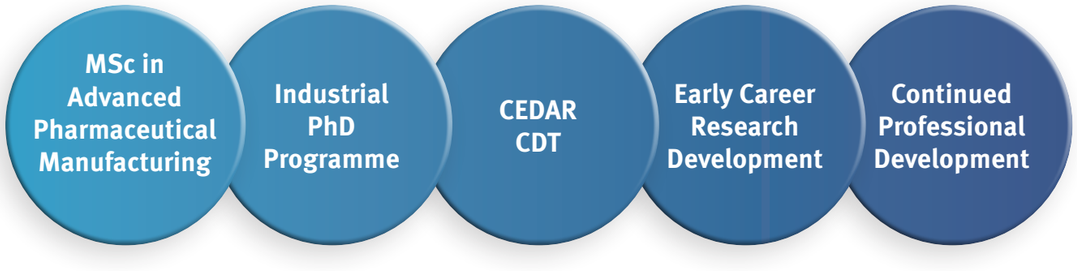


Figure 29: Range of training in CMAC Skills Pillar

MSC TRAINING

Since 2013, the University of Strathclyde has offered the MSc in Advanced Pharmaceutical Manufacturing to address the rising demand for expertise in the field. Graduates are equipped for roles in food, chemical, and pharmaceutical industries or further academic pursuits. The curriculum, developed in collaboration with industry partners, is taught by CMAC academics, researchers, and industry guest lecturers. This course focuses on producing highly skilled graduates in advanced drug substance and drug product pharmaceutical manufacturing, encompassing continuous manufacturing, digital design, formulation science, process analytical technology, and advanced process control.

26 MSc advanced pharmaceutical manufacturing students graduated in 2023-2024

"CMAC played a pivotal role in my professional life. Through interactions with pharmaceutical companies and universities, as well as the guidance of dedicated academics and researchers, I was able to not only complete my PhD, but also launch a successful career in the industry. I am proud to have been a part of such a supportive and innovative community. "

LAURA PEREIRA DIAZ,
CMAC PHD GRADUATE

PHD TRAINING

The CMAC PhD programme seamlessly integrates dynamic cross-disciplinary training with industry-tailored research projects.

The bespoke training emphasises concurrent researcher development and academic projects throughout the entire studentship. In the first year, a comprehensive formal training program, including seminars and lab workshops delivered by CMAC academics, researchers, and industry partners, equips students with theoretical knowledge, hands-on laboratory skills, and essential transferable skills. This solid foundation ensures success and progression through the research-oriented phases of their PhD programme. Over 100 training hours were delivered in 2024.

Image: Summer School 2024

In 2024, the CMAC Annual Summer School provided researchers with essential tools and skills to boost their confidence and competencies in innovation and commercialisation. Additionally, participants gained practical knowledge of Cyber-Physical Systems (CPS). It was inspiring to witness researchers exploring a new tool for measuring particle size distribution in powders and celebrating their achievements during the poster session.

Image: Training workshop

INDUSTRY ENGAGEMENT

During the doctoral training programme, students have research placements at Tier 1 pharmaceutical partners, shaping their projects and future careers. Additionally, industry-led seminars and the CMAC Open Days provide platforms for researchers to engage with industry, discuss posters, and further enrich their understanding of the pharmaceutical landscape.

TALENT PIPELINE OF DOCTORAL TRAINEES

Recruited in 2024

18 students from
4 universities

In Study in 2024

52 current students
5 on placement

Graduated

93 students, including
7 graduates in 2024

EPSRC Centre for Doctoral Training in Cyber-physical systems for Medicines Development and Manufacturing (CEDAR)

Vision: To deliver 90 highly skilled, future leaders equipped to harness the potential of cyber-physical systems and Industry 5.0 principles to transform the way that medicines are designed and made.

In April 2024 CMAC announced a new Centre for Doctoral Training (CDT) - CEDAR. Funded by UKRI, CEDAR will tackle a critical skills gap by training multi-skilled doctoral graduates equipped with advanced technical, digital and transferable skills, alongside a deep understanding of the interdisciplinary nature of medicines development and manufacturing.

Developed in collaboration with industry partners, CEDAR will train 90 future leaders with the multidisciplinary skills essential for advancing next-generation, sustainable medicines manufacturing. By developing novel Cyber-physical systems that harness the power of digital technologies including artificial intelligence, robotics and augmented reality, CEDAR will deliver the talent pipeline of future leaders who can help to bring new medicines to market effectively.

The CEDAR programme places individual students at its core, providing world-class technical training, impactful research opportunities, and the establishment of a lifelong network of peers, academic faculty, and industry experts. Graduates will embark on transformative research projects aligned with the Industry 5.0 paradigm and develop the way that cyber-physical systems can help make medicines manufacturing more sustainable, resilient and human-centric.

The programme has the support and engagement of CMAC Tier 1 Industry partners (AstraZeneca, Pfizer, Takeda, Roche, Chiesi, Lilly, UCB, and Sanofi), as well as an array of other partners, in co-developing our CDT the programme via training, project co-supervision, mentoring and placements, ensuring graduates are exposed to industry challenges and best practices. Students will also benefit from a world class research environment in the award-winning facilities at Strathclyde and our academic partners Imperial College London, the Universities of Leeds and Sheffield. This includes substantial recent investments in our digital and advanced manufacturing technologies made possible by the £33.4M UK RPIF partnership to establish the new CMAC Data Lab.

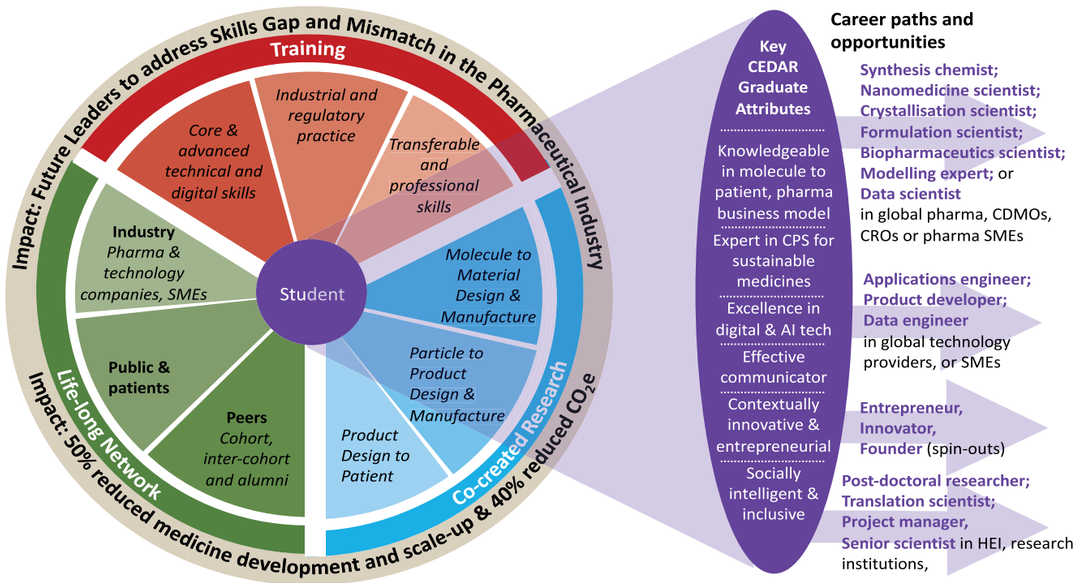


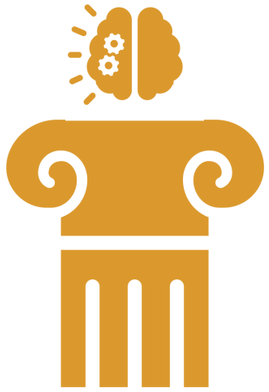
Figure 30: CEDAR overview

Image: Lab of the Future with cyber-physical systems

CEDAR Training

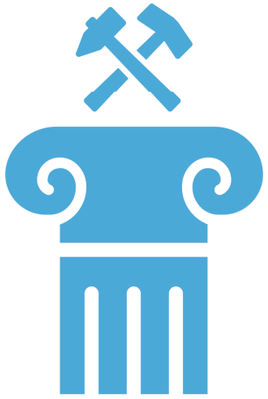
CEDAR PhD students undergo training activities aligned to the following pillars:

Multi-Disciplinary Technical & Digital Skills



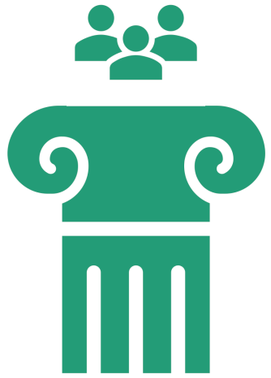
Domain knowledge
Technical skills
Digital competency

Industrial & Regulatory Practice



Development pipelines
Regulatory framework
Industry best practices

Personal Development Skills



Leadership skills
Project management
Communication skills

We welcomed our first cohort of CEDAR students in October 2024. In the first three months they completed four in person training weeks delivered at Strathclyde, Leeds and Sheffield.

The portfolio of projects, co-created with industry will collectively create a system-level, digital, and advanced processing toolbox, spanning from particle formation to biorelevant performance. CEDAR research will reveal the complex, multi-length scale relationships between molecules, particles, bulk materials, formulated products, performance, and patients. The research outcomes will accelerate the development of high-quality medicines, enhance resilience, and reduce environmental impact by leveraging cyber-physical platform technologies.

Image: CEDAR training cohort of 2024

CEDAR Research Challenge Teams

A key activity of CEDAR is cohort-based doctoral training. Each cohort is aligned with the wider CMAC programme via Research Challenge Teams.

WHAT IS A RESEARCH CHALLENGE TEAM (RCT)?

- Multiple PhD students working on projects connected by a common topic
- Multi-disciplinary group of academics and industry partners
- Benefits of collective project supervision and team development
- Training needs specific to each research challenge are identified and supported throughout the projects
- Students will work collaboratively over the course of their studies, developing skills, perspective and understanding beyond those specific to their individual project

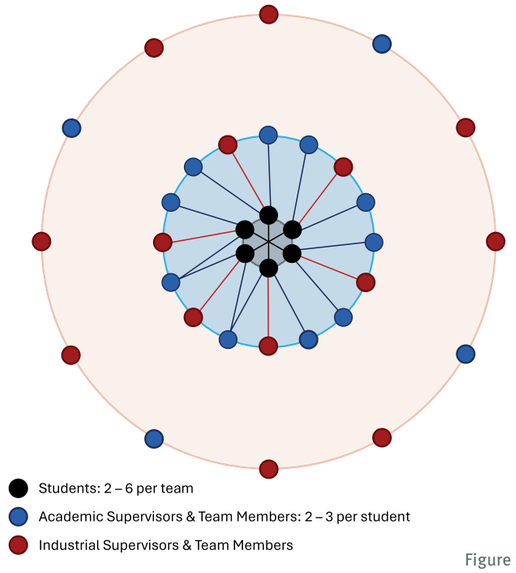


Figure 31: RCT map

RCT 1 - Microfluidic Cyber-Physical Systems for the Sustainable Manufacturing of Next-Generation Nanomedicines

Project	Researcher	Supervisor	Background	University
Rational Design of Polymeric Nanoparticles for the Delivery of Biologics for Cancer Therapy.	Sophia Kontou	Prof Clare Hoskins	Applied Chemistry & Chemical Engineering	Strathclyde
Modelling Lipid Nanoparticles – Lipid Choice and Lipid Nanoparticle Structure	Roma Fraser	Prof Yvonne Perrie	Immunology & Pharmacology	Strathclyde
Co-Delivery of Active Pharmaceutical Ingredients	Danielle O'Meara	Prof Clare Hoskins	Forensic & Analytical Chemistry	Strathclyde
Developing Digital Twins for Microfluidic Nanoparticle Manufacture	Alice Warén	Prof Jan Sefcik	Pharmacology	Strathclyde

RCT 2 – Cyber-Physical System for Drug Substance: Integrated DataFactories for Synthesis, Purification and Crystallisation Scale-Up

Project	Researcher	Supervisor	Background	University
Integrated Self-Optimisation of API Synthesis and Crystallisation Using Machine Learning: Next-Generation Pharmaceutical Process Development	Rohan Shetty	Prof Sven Schroeder	Chemical Engineering	Leeds
Crystallisation Screening DataFactory	Muhammad Asfand Awan	Prof Alastair Florence	Chemical Engineering	Strathclyde
End-to-End Process Optimisation for Impurity Rejection	Harrison Fraser	Prof Claire Adjiman	Chemical Engineering	Imperial
Data Platform and Ontologies Drug Substance CPS	Andrew Shearer	Prof Blair Johnston	Machine Learning & Deep Learning	Strathclyde
CPS for Characterisation and Control of Particle Attributes in Crystallisation Processes	Ben Timlin	Dr Javier Cardona	Chemical and Process Engineering	Strathclyde
Crystallisation Scale-Up and Optimisation	Kate Henderson	Dr Cameron Brown	Chemical Engineering	Strathclyde

RCT 3 – Cyber-Physical System for Drug Product to Patient: Integrated DataFactories Connecting Formulation Strategies, Drug Product Design and Product Performance

Project	Researcher	Supervisor	Background	University
Multi-Route DataFactory for Amorphous Solid DispersionS	Abdelazeez Mohamednour	Prof John Robertson	Pharmacy, Advanced Pharmaceutical Manufacturing	Strathclyde
Multi-Route DataFactory for Direct Compressed Products	Muhammad Murtaza	Prof Daniel Markl	Electrical Engineering	Strathclyde
Hybrid Mechanistic and Machine Learning Approaches to Product Performance Prediction	Amir Arjmandi-Tash	Dr Rachel Smith	Chemistry	Sheffield
Dissolution Release Mechanisms for Amorphous Solid Dispersions	Rebecca Hardman Carter	Prof Daniel Markl	Molecular & Cellular Biology, Bioinformatics	Strathclyde
TIM-1 Model: Predicting Absorbable Dose & Crystallisation Strategy	Scott Reid	Dr Hannah Batchelor	Pharmacology	Strathclyde
Deciphering Dissolution Dynamics: Building a Digital Model of TIM-1 Apparatus	Santhiya Thiagarajan	Dr Cameron Brown	Biotechnology, Advanced Drug Delivery	Strathclyde

Continued Professional Development

EARLY CAREER RESEARCHER DEVELOPMENT

CMAC's Early Career Researchers (ECRs), engaged in UKRI or industry-funded projects, benefit from a wide array of career development opportunities.

A standout event was Creativity@Home, which empowered our researchers to grow their mindset, personal branding, and strategic networking.

INTRODUCTION TO CMAC SKILLSFACTORY

The CMAC SkillsFactory will be a training hub for the small molecules medicines manufacturing sector, offering resources tailored to diverse learner needs. To date the platform has been used by CDT students and will be launched to external users in 2025.

The platform includes learner pathways in digital Chemistry, Manufacturing, and Control (CMC): CMAC-delivered online and practical courses and live training with experts. Future features will include transferable skills training, on-boarding for new CMAC staff, personal training records, and STEM engagement materials.

The platform integrates various formats to create an engaging learning environment: interactive courses with quizzes and exercises, expert-led webinars, live online classes fostering collaboration, XR training for immersive experiences, discussion forums for peer learning, and supplementary materials like articles and case studies.

In-person practical courses will also complement online learning to enhance hands-on skills, ensuring the platform meets learner needs while fostering career growth in digital CMC.

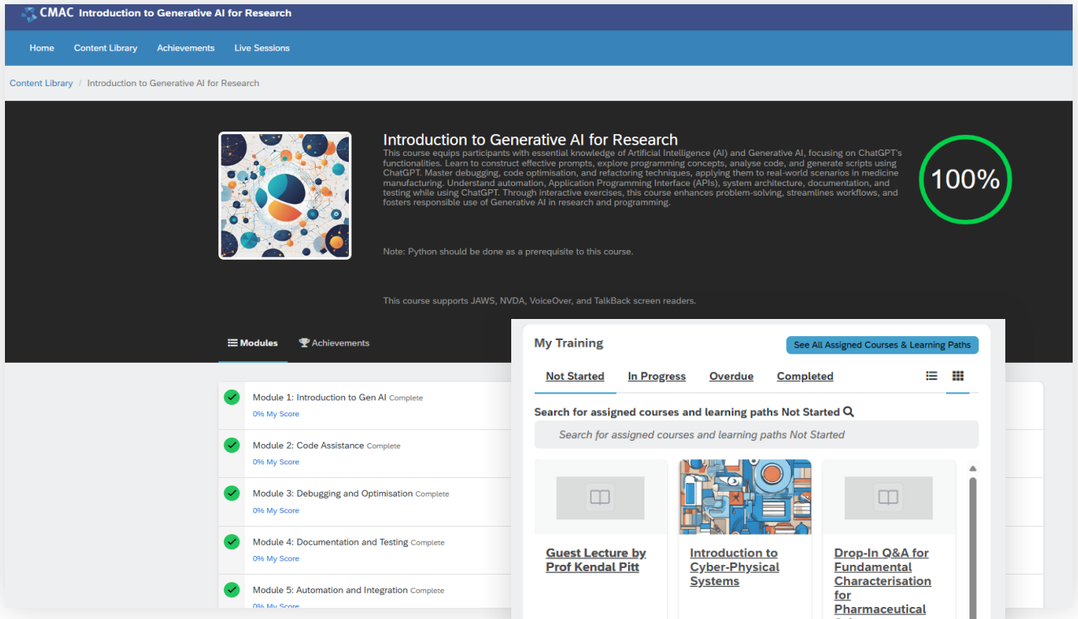


Figure 32: CMAC SkillsFactory user interface

World Class Facilities

"The CMAC facilities at the University of Strathclyde remain at the forefront of all our activities and offer unparalleled research capabilities. 2024 saw the beginning of the £11 M UKRPIF Data Lab capital investment take shape with many installations and new technologies already underway. There has also been a significant infrastructure development with the commissioning of the Cyber-Physical Research & Development Data Lab which features a number of advanced automation platforms.

With the overall headcount for CMAC Strathclyde now exceeding 150, our dedicated National Facility team has a more significant role than ever in supporting the various programmes across our portfolio. The team continue to provide services and training, in addition to supporting and maintaining our world-leading instrumentation"

Dr Thomas McGlone,
Senior Technical Operations & Tier 2 Manager

Image: CMAC National Facility Technical staff at CMAC Open Days 2023

NATIONAL FACILITY 2024 OUTPUTS:

5
SMEs supported

>35
Projects for industry

>100
Researchers supported

£5m
In existing equipment upgraded or new equipment installed

CMAC National Facility

UNIVERSITY OF STRATHCLYDE

The award winning CMAC National Facility at the University of Strathclyde has unparalleled research capabilities to identify, understand, monitor and control critical aspects of advanced pharmaceutical manufacturing research. The facility is closely aligned with the latest research in innovation, which provides an efficient means of translation to industry. These services include a comprehensive suite of drug substance and drug product batch and continuous processing equipment, novel monitoring and control systems and extensive off-line characterisation capabilities.

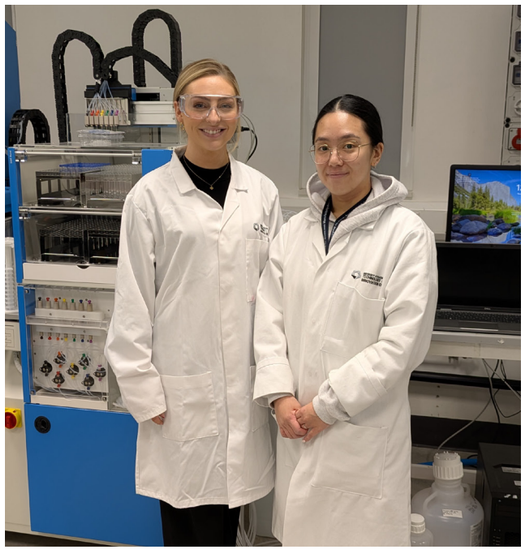


Image: Researchers at CMAC National Facility in Glasgow

Academic Support

CMAC is built upon a collaborative ethos whether working with multidisciplinary local academic teams or international researchers. The National Facility team plays a critical role in supporting this by working to support individual researchers to access and use the facilities or in the provision of research services. One PhD student said "The National Facility Team have been instrumental in supporting my research, providing not just standard instrument training but also experimental guidance and technical expertise. I could not have delivered my project to the same standard without their help."

Sotax fully automated dissolution testing platform

There have been a number of significant capital investments in the CMAC facilities this year as part of the UKRPIF Data Lab programme including a £350 K automated dissolution testing platform from Sotax. This state-of-the-art system is the first installation of it's kind in an academic environment and will greatly enhance our dissolution analysis capabilities, supporting a wide range of projects across the CMAC portfolio. During commissioning, it was essential to work closely with Merck to ensure the correct throughput of purified water for the preparation, analysis and discharge of dissolution media. The system allows 100 % unattended dissolution runs including media preparation, vessel filling and self-cleaning. Results can be determined in real-time with integrated UV-Vis and/or via the collect of samples for offline HPLC.

Industry Access

Our facility team is fully established and ready to undertake projects across the CMAC portfolio. We are operational in five distinct technical areas, supported by lead academics and complementary functions These areas are:

- Crystallisation & Particle Engineering
- Drug Product
- Solid State
- Advanced Analytical
- Nanomedicines

Over the past year, our team has successfully executed a wide array of projects for clients, encompassing the understanding and development of crystallisation processes, particle engineering to enhance physical properties, advanced material characterisation, and the production and analysis of lipid nanoparticles. Additionally, we have expanded our expertise in the drug formulation space, delivering impactful solutions in this critical area.

Work with us

- To conduct applied research in process development, particle engineering and advanced analytical services
- To engage with a dedicated team of highly skilled development and characterisation scientists
- To gain access to a world class manufacturing research facility with extensive equipment capabilities

Our teams are fully established and ready for collaboration. Feel free to contact us at

cmac-national-facility@strath.ac.uk

CMAC DATALAB

A Digital Medicines Manufacturing Research Accelerator

The CMAC Data Lab is an £11M capital award as part of a £33.4M funding initiative from UK Research Partnership Investment Fund (UKRPIF) to advance research infrastructure and accelerate innovation in medicines manufacturing. This will facilitate the development of a CMAC Data Fabric to capture all data, build unique data assets and develop predictive modelling solutions to:

- Drive the digital transformation of Chemistry, Manufacturing and Controls (CMC)
- Achieve Industry 5.0 goals of Sustainability, Resilience and Human-Centricity

In 2024, 38 new state-of-the-art instruments were successfully installed and commissioned, marking a significant leap forward in research capabilities. These world leading research tools are now integral to a diverse array of pioneering academic and industrial research projects, including UKRI, EPSRC and BBSRC funded PhDs, DDMAP, DM2, SolvIT, CMAC Hub , MediForge, CEDAR and Prosperity Partnership projects, as well as industry funded Core projects and 10 National Facility projects. The introduction of these instruments and their innovative techniques has not only increased R&D productivity, speed and agility for product and process development, but they have played a vital role in enhancing the skills of both staff and students, ensuring a future-ready workforce. These advancements have also strengthened strategic industry partnerships and increased investment in research income from industry partners.

Image: Lab of the Future

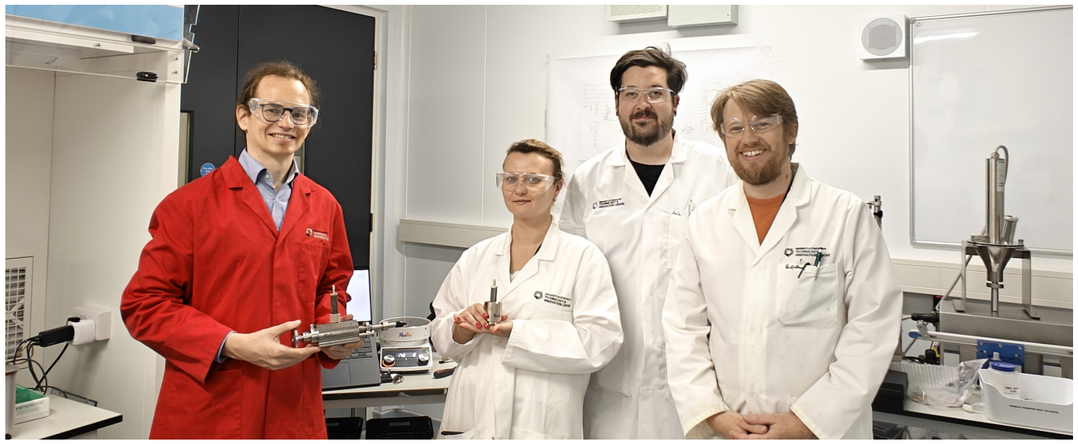


Image: Researchers benefitting from new Data Lab equipment

NETZERO

Medicines Manufacturing Research Pilot

CMAC Net Zero Pilot Areas

- Reduced energy consumption by switching to energy efficient infrastructure and equipment
- Reduced chemical waste by using smart, intelligent, small scale experimental platforms
- Reduced emissions from travel by adopting the latest immersive digital tools to enhance collaboration

In 2022, CMAC was awarded funding of £2.5 million for the UKRPIF Net Zero Medicines Manufacturing Research Pilot from Research England and the Scottish Funding Council. With a project duration spanning 2022 - 2027, this capital award supports CMAC's 2021-26 Strategy and commitment to developing sustainable processes and technologies for future medicines manufacturing.

The Net Zero Pilot has largely been focussed on the following key areas:

Infrastructure:

- Lab infrastructure upgrades
- Replacement of energy inefficient instrumentation
- Energy and waste monitoring
- Smart experimentation and automation

Figure 33: NetZero - CMAC travel emissions in 2023 and 2022

As part of the project we have implemented an annual travel survey for staff and students to better understand our environmental impacts. This is well aligned with the recent University travel policy which is a critical part of the Institution's broader NetZero targets.

As a world leading centre with an extensive network of international contacts, travel remains an important aspect of our operations however the following approaches have been put in place:

- All travel has additional review measures to assess if essential or not
- Air travel is restricted for domestic trips
- Essential international travel is coordinated to cover multiple purposes rather than individual
- Internal and external meetings with individuals from multiple sites have the option of taking place remotely
- A dedicated meeting facility with advanced communication features has been set up in the TIC building

Recognition

CMAC received a special mention in the sustainability category at Scotland's Life Sciences Annual Awards and Dinner in March 2024.

Image: CMAC team at Scotland's Life Sciences Annual Awards in 2024

Facilities and Capability in MediForge Spokes

The MediForge Hub is hosted within CMAC: a world-class, award winning research environment at University of Strathclyde. Substantial equipment investment has created a unique world class research facility, including a £33M UKRPIF partnership in 2013, a £2.5M UKRPIF Net Zero Pilot in 2021 that enabled waste and energy monitoring infrastructure and a £34M UKRPIF Round 7 partnership in 2023 that secured £11M for CPRI hardware.

State-of-the art facilities across the spokes provide additional facilities and expertise in cyber-physical systems and digital technologies across all partners.

Image: Tabletting DataFactory at Strathclyde with XR add-on built by Glasgow School of Art

GLASGOW SCHOOL OF ART

Human-machine Interfaces, XR and Data Visualisation

GSA's involvement with DM² and MediForge showcases its expertise in developing interactive digital systems, particularly in advanced 3D modeling and XR (extended reality) applications. With a focus on creating highly detailed and functional Digital Twins, GSA leverages its multidisciplinary strengths across human-computer interaction (HCI), visualisation, psychology, and immersive technologies to foster innovative and impactful solutions.

GSA brings years of experience partnering with CMAC. Example projects include virtual reality (VR) training systems for complex laboratory equipment, augmented reality (AR) visualisations, novel approaches to visualise and interact with multidimensional / multivariate data, and educational tools catering to audiences from primary school children to researchers. GSA's facilities, available to CMAC, include separate XR, audio recording, and usability laboratories designed to analyse user interaction with new systems. Their robust infrastructure ensures the delivery of high-quality, user-centered solutions.

IMPERIAL COLLEGE LONDON

Multi-scale modelling and optimisation methods, sustainable process manufacturing

The Sargent Centre for Process Systems Engineering, a joint research centre at Imperial and University College London develops models and methods to support decision-making in the development and operation of industrial processes. Models and methods are captured in the Sargent Centre's Digital Systems Library, in the form of databases, model input files and in-house software. Taking advantage of the transferability of the models and tools developed, the Digital Systems Library is used in a variety of collaborative research projects, with industry partners, including members of the Sargent Centre's Industrial Consortium, and other academic institutions.

The broad scope of the Sargent Centre's Digital Systems Library makes it useful to support decision-making at different scales and across scales, thanks to the use of multiscale models. Models include thermodynamic property modelling of crystalline and fluid phases, transport and kinetics, specific process operations such as reactors, membrane contactors, crystallisation, chromatography, and whole-systems design including end-to-end processes or complex supply chains.

The Centre team advances the development of a range of technologies (machine learning, optimisation, mechanistic modelling, uncertainty quantification) to tackle pressing problems in pharma and biopharma, such as Quality by Digital Design, design space exploration, experiment design, online monitoring and control, and risk management. The Digital Systems Library has been used across industrial sectors, including pharma, agrochemicals, energy, FMCG and is complemented by a set of training courses for practitioners. For CMAC, the facility has been used to advance solubility prediction capabilities with the state-of-the-art SAFT-γ Mie approach and to support the QbDD initiative with new solvent design tools.

UNIVERSITY OF LEEDS

The Leeds team links the MediForge community of researchers to digital manufacturing research infrastructure in the Institute of Process Research and Development (https://www.iprd.leeds.ac.uk/) at Leeds.

IPRD core facilities include:

- Custom-built flow chemistry equipment for continuous processing
- Process analytical technologies (PAT) (FTIR, turbidity, pH, UV-vis, mass spectroscopy, GC, HPLC) for inline and online reaction monitoring
- PAT-instrumented 20 and 50 litre batch reactors for process development and scale-up
- Reaction and parallel calorimeters for chemical hazard and reaction progress Process development separation and isolation equipment

Both the Bourne (https://www.bournelab.co.uk) and Schroeder (http://www.slmslab.info) labs are members of Institute of Process Research and Development, with the former providing world-leading capability in designing automated self-optimising reactors for multistage processes and the latter pioneering the use of advanced process analytical technologies in national facilities such as the Henry-Royce Institute (https://www.royce.ac.uk), the Bragg Centre at Leeds (https://www.leeds.ac.uk/bragg-centre-materials-research) and Diamond Light Source (https://www.diamond.ac.uk) on the UK Science and Innovation Campus at Harwell for applied manufacturing research. Combined, these capabilities provide MediForge with world-wide unique infrastructure for digital chemical manufacturing through structure/reactivity and structure/performance relationships.

Image: DiPP at Sheffield

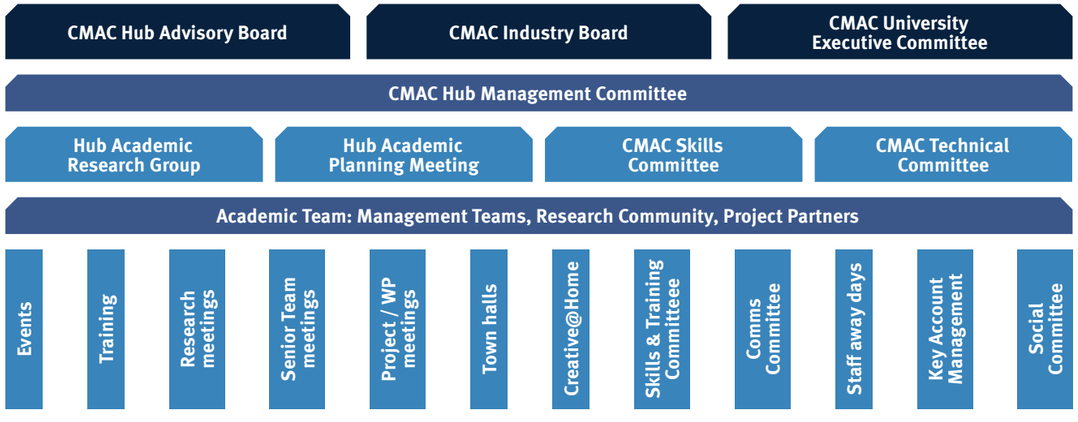
UNIVERSITY OF SHEFFIELD

Production-scale Drug Product Manufacturing, Robotics and Automation, Sustainable Process Manufacturing

The team at the University of Sheffield have excellent facilities for both experimental and computational research in drug product manufacturing and performance. In addition to extensive facilities for lab scale research and characterisation, the Diamond Pilot Plant (DiPP) at the University of Sheffield houses cutting edge pilot scale manufacturing equipment, available for teaching and research activities. The GEA Consigma 25 wet granulation and tabletting line is the first of its scale at any UK University and enables transformative research for continuous pharmaceutical manufacturing at pilot to full manufacturing scale, in both physical and digital domains. The facility is well supported with a suite of powder and product characterisation equipment and expert operators. The team also possess world class computational simulation expertise in the fields of population balance modelling (PBM) and discrete element method (DEM), enabling complementary simulation and experimental data generation to advance pharmaceutical manufacturing research.

CMAC Governance Structures

CMAC HUB GOVERNANCE STRUCTURES



HUB ADVISORY BOARD (TO SEPT 2024)

Name	Organisation
Dr Amy Robertson	AstraZeneca
Dr Nigel Westwood	Cancer Research UK
Mr Paul Blakeman	Centre for Process Innovation
Dr Dave Tudor	Centre for Process Innovation
Dr Walkiria Schlindwein	De Montfort University
Dr Laura Totterdell	EPSRC UKRI
Prof Nilay Shah	Imperial College London
Dr Sarah Goulding	Innovate UK
Dr Adam Fine	Merck Sharp and Dohme
Prof Ian Gilmore	National Physical Laboratory
Dr Sean Bermingham	Siemens
Mr Johnathon Marshall	PwC
Prof Paul N Sharratt	Singapore Institute of Technology (Chair)
Prof Richard Hague	University of Nottingham
Prof Clive Badman	University of Strathclyde
Mr Massimo Bresciani	EPSRC Hub University of Strathclyde
Ms Helen Feilden	EPSRC Hub University of Strathclyde
Professor Alastair Florence	EPSRC Hub University of Strathclyde
Miss Lorna Gray	EPSRC Hub University of Strathclyde

CMAC INDUSTRY BOARD

Name	Organisation
Catherine Boissier	AZ
Andrea Casazza	Chiesi
Alastair Florence	CMAC
Massimo Bresciani	CMAC
Rebekah Russell	CMAC
Chris Burcham	Eli Lilly
Sarah O'Keeffe	Eli Lilly
John Mack	Applied Materials
Neil Dawson	Pfizer
Olivier Drap	Pfizer
Robert Yule	Sanofi
Pirmin Hidber	Roche
Charles Papageorgiou	Takeda
Jérôme Mantanus	UCB
Graham Wren	University of Strathclyde

CMAC HUB ACADEMIC RESEARCH GROUP (TO SEPT 2024)

Professor Alastair Florence
Director
University of Strathclyde

Massimo Bresciani
Industry Director
University of Strathclyde

Professor Blair Johnston
Associate Director (Academic)
University of Strathclyde

Dr Daniel Markl
Associate Director (Academic)
University of Strathclyde

Dr John Robertson
Associate Director (Academic)
University of Strathclyde

Dr Rebecca Dean
Funding and Finance Manager
University of Strathclyde

Dr Ian Houson
Technical Portfolio Manager
University of Strathclyde

Helen Feilden
CMAC Hub Project Manager
University of Strathclyde

Dr Jonathon Moores
CMAC Technical Translation Manager
University of Strathclyde

Dr Ettore Settanni
University of Cambridge

Dr Jag S. Srai
University of Cambridge

Professor Amparo Galindo
Imperial College London

Professor Claire Adjiman
Imperial College London

Professor George Jackson
Imperial College London

Dr Brahim Benyahia
Loughborough University

Professor Chris D. Rielly
Loughborough University

Dr Wei Li
Loughborough University (to March 2024)

Professor Sven Schroeder
University of Leeds

Professor Jim Litster
University of Sheffield

Dr Rachel Smith
University of Sheffield

Professor Alison Nordon
University of Strathclyde

Dr Chantal Mustoe
University of Strathclyde

Dr Cameron Brown
University of Strathclyde

Professor Chris Price
University of Strathclyde

Dr Elke Prasad
University of Strathclyde

Professor Gavin Halbert
University of Strathclyde

Professor Jan Sefcik
University of Strathclyde

Dr Javier Cardona
University of Strathclyde

Dr John McGinty
University of Strathclyde

Dr Magdalene Chong
University of Strathclyde

Dr Murray Robertson
University of Strathclyde

Dr Alice Turner
University of Strathclyde

TECHNICAL COMMITTEE

Company	Members
AZ	Amy Robertson, Gavin Reynolds, Helen Wheatcroft
Chiesi	Alessandro Falchi, Alessandro Picinnini
CMAC	Alastair Florence, Aruna Prakash, Jonathan Moores, Massimo Bresciani, Rebekah Russell
Eli Lilly	Chris Burcham, James Wyatt Roth, Jeremy Miles Merritt, Joel Calvin, Jonathan Wade, Youlin Liu
Pfizer	Kevin Girard, Paul Meenan, Martin Rowland
Roche	Marcello Bosco, Pirmin Hidber, Susanne Page, Michael Juhnke
Sanofi	Robert Yule, Sophie Martin
Takeda	Charles Papageorgiou, Marianne Langston, Neda Nazemifard
UCB	Jérôme Mantanus, Ugo Cocchini, Efty Hadjitoffis

Image: Living Lab

RESEARCH PORTFOLIO PROJECTS ACADEMIC TEAMS

MEDIFORGE HUB (FROM OCTOBER 2024)

University	Name
University of Strathclyde	Prof Alastair Florence, Director Prof Blair Johnston Prof Daniel Markl Prof John Robertson Prof Alison Nordon Dr Cameron Brown Prof Jan Sefcik Dr Javier Cardona
Glasgow School of Art	Prof Paul Chapman Dr Steve Love
Imperial College London	Prof Amparo Galindo Prof Claire Adjiman Prof George Jackson
University of Leeds	Prof Richard Bourne Prof Sven Schroeder
University of Sheffield	Prof Rachel Smith

COMMUNITY FOR ANALYTICAL MEASUREMENT SCIENCE (CAMS) FUNDED UNDERSTANDING LONG- TERM STABILITY OF SOLID PHARMACEUTICAL DOSAGE FORMS

University	Name
University of Strathclyde	Prof Daniel Markl Dr Ibrahim Khadra

CEDAR CDT

University	Name
University of Strathclyde	Prof Alastair Florence Prof Daniel Markl Prof Clare Hoskins Prof Yvonne Perrie
Imperial College London	Prof Claire Adjiman
University of Leeds	Prof Sven Schroeder
University of Sheffield	Prof Rachel Smith

CERSI

University	Name
University of Strathclyde	Prof Alastair Florence Prof Daniel Markl Prof Clare Hoskins Prof Yvonne Perrie

CORE PROJECT: SCALE UP CRYSTALLISATION DATAFACTORY

University	Name
University of Strathclyde	Dr Cameron Brown Dr Thomas Pickles

CORE PROJECT: SPHERICAL AGGLOMERATION

University	Name
University of Strathclyde	Dr Kenneth Smith Dr Bilal Ahmed Dr Martin Prostredny

DIALLING UP PERFORMANCE FOR ON DEMAND MANUFACTURING (3DP)

University	Name
University of Strathclyde	Prof Alastair Florence Prof Blair Johnston
Nottingham	Prof Ricky Wildman Dr Yinfeng He Dr Anca Pordea Prof Ian Ashcroft Prof Clive Roberts Prof Morgan Alexander Prof Cameron Alexander Prof Derek Irvine Dr Felicity Rose Dr Anna Croft Prof Richard Hague Prof Christopher Tuck
Reading	Prof Wayne Hayes
Cambridge	Prof Roisin Owens Prof George Malliaras
Partners	CPI IBioIC

DIGITAL DESIGN AND MANUFACTURE OF AMORPHOUS PHARMACEUTICALS (DDMAP)

University	Name
University of Strathclyde	Prof Alastair Florence Dr Cameron Brown Prof Blair Johnston Prof Daniel Markl Prof John Robertson
Ghent	Prof Thomas De Beer Prof Ashish Kumar
Copenhagen	Prof Annette Müllertz Prof Thomas Rades Prof Jukka Rantanen

DPN-MED

University	Name
University of Strathclyde	Prof Alastair Florence Prof Blair Johnston Prof Daniel Markl

GASTROINTESTINAL BIOREACTOR TO EVALUATE INGESTIBLE MEDICINES AND INFORM FORMULATION AND MANUFACTURE (GIBIO)

University	Name
Strathclyde	Dr Hannah Batchelor Prof Alastair Florence Linda Horan Dr Ibrahim Khadra Prof Stephen McArthur

KTP WITH AZ

University	Name
Strathclyde	Prof Daniel Markl Dr Cameron Brown

KTP WITH GSK

University	Name
Strathclyde	Prof Daniel Markl Dr Cameron Brown

MADE SMARTER INNOVATION - DIGITAL MEDICINES MANUFACTURING RESEARCH CENTRE (DM^2)

University	Name
Strathclyde	Prof Alastair Florence Massimo Bresciani Prof Blair Johnston Prof Daniel Markl Prof Gareth Pierce
Loughborough	Dr Brahim Benyahia Cambridge Dr Jagjit Srai

MMIC GRAND CHALLENGE 1

University	Name
Strathclyde	Prof Daniel Markl Prof John Robertson

PHARMACRYSTNET

University	Name
Strathclyde	Dr Cameron Brown Prof Blair Johnston Dr Victorita Dolean Maini

PROSPERITY PARTNERSHIP THEME 4 WITH GSK

University	Name
Strathclyde	Dr Cameron Brown Prof Alastair Florence Prof Blair Johnston Prof John Robertson
Nottingham	Prof Ricky Wildman Dr Ender Ozcan Dr Derek Irvine Dr Anna Croft

RIGHT FIRST TIME MANUFACTURE OF PHARMACEUTICALS (RIFTMAP)

University	Name
Sheffield	Prof Jim Litster Prof Daniel Coca Prof Mahdi Mahfouf Prof Agba Salman
Strathclyde	Prof Blair Johnston Prof Daniel Markl
Purdue	Prof Gintaras Reklaitis Prof Marcial Gonzalez Prof Zoltan Nagy

SHARPEN

University	Name
University of Strathclyde	Prof Blair Johnston

SUSTAINABLE PHARMACEUTICAL MANUFACTURING: COMPUTER AIDED SOLVENT DESIGN TO MINIMISE SOLVENT USE ACROSS INTEGRATED SYNTHESIS, PURIFICATION & ISOLATION (SOLVIT)

University	Name
Strathclyde	Prof Chris Price Prof Jan Sefcik Prof William Kerr Dr David Lindsay Dr Jun Li
Imperial	Prof Claire Adjiman Prof Amparo Galindo Prof George Jackson

Image: Living Lab

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