CMAC Strategy

2021-26

CMAC

Foreword

CMAC is an internationally leading manufacturing research centre that has a unique configuration of academic research, applied and pre-competitive programs. Working in close partnership with our Tier 1, Tier 2, academic and innovation partners over the last 10 years we have established a vibrant portfolio of multi-disciplinary collaborative research, training and translation projects within a world class facility. As we pass the 10th anniversary of the Centre it has provided us with an excellent opportunity to take stock of what has been achieved, reflect on developments across the national and international medicines ecosystem and, crucially, to review and update our scope and priorities. Working together we have refreshed our strategy to inform the next phase of the Centre's development geared to deliver benefits to all our partners and to provide value to the wider society we serve and, ultimately, patients.

We are delighted to present CMAC's 2021-26 strategy and invite you to contact us to discover how you can co-create disruptive solutions, co-deliver leading research, and drive forward the future of medicines development and manufacture.

Contents

1. Executive Summary

CMAC: A global research and development Centre for Advanced Manufacturing of Medicines.

The pharmaceutical industry faces the global challenge to enhance the development and manufacture of medicines to be faster, more cost effective and productive, to embed sustainability and to deliver improved security of supply whilst still assuring the quality and safety of medicines to patients. Building on 10 years of successful operation, CMAC's collaborative program aims to co-create and co-deliver the new science, innovative process, digital technologies and future workforce that will enable the adoption of advanced science and technology to transform product and process development and medicine manufacturing to enable future medicine supply.

We will deliver across four satrtegic pillars of 1) Research excellence and intensity, 2) Outstanding skills development, 3) World class facilities and 4) Exemplary translation to industry. We seek to build on our collaborative model to partner with industry, academia and others to accelerate progress across these critical areas and deliver real impact.

Our exciting research strategy places advanced particle formation and control as a central target that can enable the disruptive benefits from more closely linked knowledge across drug substance and drug product manufacturing. This will be achieved through delivering better understanding of the relationships and interdependencies between materials, structure, properties through to processes and how these dictate manufacturability, stability and performance in patients.

To achieve our end-to-end system level view our scope considers synthesis, through purification and isolation to formulation and secondary product manufacture, distribution and use. We will connect end users and technology providers with leading research teams to co-create innovative Cyber-Physical Systems that embed Industry 4.0 principles and industrial digital technologies to realise benefits from digital design, advanced process technology and data-driven manufacture and control.

Our integrated approach to enabling advanced processing and the digitalisation of key stages of chemistry, manufacture and control (CMC) operations includes:

- **Quality by Digital Design (QbDD) Digital workflows that combine powerful new predictive methods for crystallisation, drug product manufacture and biorelevant design.**
- **Digital Twins for medicines development and manufacture that encompass the data, models and knowledge that describe the materials, products and processes across our program.**
- **Smart, data driven DataFactory development platforms to develop, optimise and validate models harnessing developments in automation, robotics, measurement, sensors and data science to deliver innovative mechanistic, Machine Learning (ML) / Artificial Intelligence (AI) and hybrid approaches.**
- **Integrated small scale, flexible, modular continuous processing platforms or MicroFactories to convert optimised process designs from the Digital Twin into right first time, on demand production platforms.**

Together these advances will deliver quality, speed, cost, sustainability and security of supply improvements and the associated benefits of predictive development, right first time manufacture and future digital technology. We will continue to invest in our facilities and technology base to support the advances and ensure an excellent environment to support both world class research and high quality training. Our training programs will continue to deliver a talent pipeline with key skills attributes necessary to overcome the barrier in achieving translation and adoption of industrial digital technologies. Crucially our strategy embeds translation to industry at every level from co-creation through co-delivery ensuring we maximise the impacts and benefits to all of our partners, the wider economy, the environment and ultimately patients.

2. 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, the urgency for Net Zero and to realise the economic and social benefits from a robust, sustainable medicines manufacturing sector, able to rapidly translate breakthroughs in medical science to patient benefit.

To achieve this goal we must:

- develop new science and engineering knowledge and tranlsate it effectively to generate value
- deliver digital transformation of Chemistry, Manufacturing and Control (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. 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

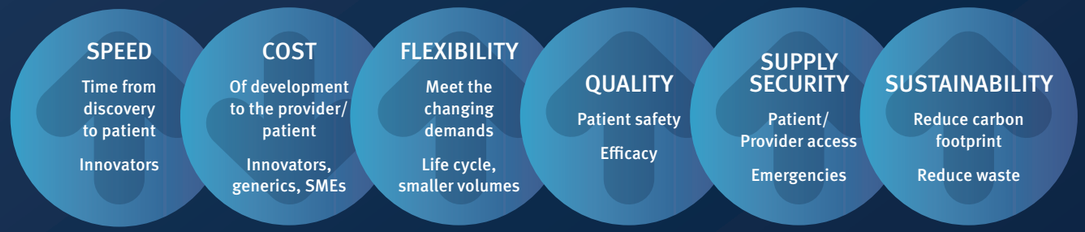
Accelerate pace of manufacturing innovation through understanding the needs of:

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:



3. Vision, Mission & Strategic Goals

VISION

To be a globally leading research centre to transform medicines development, manufacture, and supply.

MISSION

To deliver value to our stakeholders by creating the new science, innovative technologies & future workforce that will support the adoption of advanced CMC development, digital technologies and manufacturing approaches to enable future drug substance & drug product supply.

PILLARS AND STRATEGIC GOALS

CMAC will focus on delivering our strategic priorities for Research and for the Centre. We will achieve this by (i) continuing to focus on strengthening collaborative partnerships across the research and innovation ecosystem and (ii) growing a diverse, sustainable program portfolio across our four pillars:

Research Excellence & Intensity

Outstanding Skills Development

World Class Facilities

Exemplary Translation to Industry

Strategic Research Priorities

1 Accelerate Development

- Design sustainable continuous processes for API & DP with minimal material
- Useful predictive tools for product and process development
- DataFactories: Smart, autonomous, AI-driven development platforms

2 CMC Digitalisation

- Digital Twins of materials, products & process
- Multiscale, multiphysics and hybrid modelling for CCS, MCS+, BPCS and QbDD
- Accessible CMAC toolbox of IDTs (ML/AI, AR/VR, robotics) in development & manufacture

3 Advanced Manufacture & Supply

- Innovative continuous processing
- Integrated solutions across API and DP: flexible, modular MicroFactories
- Real time control and release
- Sustainability as value

4 Materials & Products

- Pharmaceutical materials science underpinning stability, manufacturability and performance
- Structure property relationships from molecule ⟿ crystal/particle ⟿ bulk ⟿ formulated product

Strategic Centre Priorities

1 Lab of The Future

- Cutting edge facilities
- Support portfolio of basic and applied research, talent pipeline, Digital Twins, DataFactories, MicroFactories, intelligent Workflows & materials science
- Facilitate collaboration, innovation & translation

2 Future Workforce

- Delivering the highly skilled, augmented workforce of the future.
- Future research leaders for industry & academia
- Sector leading CMAC talent pipeline of 'industry ready' recruits

3 Translation & Impact

- Demonstrate case studies & advocate business case for continuous & advanced manufacturing
- Network & engage with global stakeholders including regulators
- International presence

4 World Leading Centre

- Grow position as global manufacturing research centre
- Case studies and business case for Continuous Manufacturing (CM)
- Grow and manage sustainable portfolio of funded research and translation activities
- Attract global talent

Values

We are guided in executing our strategy by the values that make the centre a great place to work; an excellent, responsive partner in all our collaborations and a trusted and valued organisation in the UK and international medicines research and innovation ecosystem. We will embolden our staff and students to take on risky challenges; we will learn together from our failures and celebrate the successes we achieve together.

COLLABORATIVE: Inter-disciplinary science driven by research excellence and integrity through co-creation and co-delivery of our portfolio

INCLUSIVE: Realising our potential through equality diversity and inclusion (ED&I) active engagement and collaboration with stakeholders, embedding the principles of public life, sustainable development goals (SDGs) and Responsible Research & Innovation in how we deliver our portfolio

AMBITIOUS: Impact Focussed Research and Innovation drive us as we strive to maintain and develop both research excellence in our training and research and operational excellence as a leading manufacturing research centre

PEOPLE ORIENTED: Open and inspirational culture & environment, supporting staff and students to reach their full potential across our research, skills, facilities and translation pillars

4. CMAC: A world leading collaborative R&D centre for medicines manufacturing research

CMAC is building on 10 years of experience as a pre-competitive collaborative R&D centre to continue to develop our established portfolio of funded programmes across our scope and Technology Readiness Levels (TRLs) in medicines development and manufacturing.[4]

Industry Drivers

- Speed
- Cost
- Flexibility
- Quality
- Supply Security
- Sustainability

Common Industry Interests:

- Accelerated development and approval
- Advanced Manufacturing Technology including continuous
- Scale Down, distributed manufacturing
- Digitalisation and Industry 4.0 for design and manufacture
- Material science and advanced characterisation Sustainability

Award Winning Facilities

Expert Staff

Portfolio

To Deliver Benefits to:

Medicines manufacturing community Tier 1, Tier 2, regulators and patients:

- Accelerated Innovation
- Co-Created Research
- Research Expertise
- World Class Facilities
- Responsive R&D Services
- Talent Pipeline

Benefits to: UoS/HEIs:

- Research Intensity And Quality
- Industry Engagement
- Impact
- Income & Investment

Requires Growth in:

- **STAFF:** academic, technical, support
- **FACILITIES:** infrastructure, equipment and technology
- **INCOME:** research, training, translation
- **MARKET SHARE:** internationalisation, UK
- **PARTNERSHIPS:** best with best collaborations

Transformative solutions aligned with core values and global challenges

By continuing to build on our core strengths and partnerships our research will be internationally leading, disruptive and impactful.

Our portfolio of research, training, facilities and translation is:

INFORMED
by the global challenges facing those involved in the development, manufacture and supply of medicines. We are informed by sector wide strategy including industry 4.0 and sustainability.

ALIGNED
with the common interests of our industry partners and stakeholders across the medicines value chain and critical global needs to achieve Net Zero.

COLLABORATIVE
working in partnership across the Research and Innovation ecosystem to accelerate progress and leverage excellence and strength.

IMPACTFUL
inspired by the needs of our partners and end users, executed to the highest standards and focussed on translating the outputs of our research to benefit all our stakeholders from Tier 1 and 2 industry partners to patients.

SUSTAINABLE
delivering improvements in how we can reduce waste, material and energy consumption across the value chain.*

Across CMACs portfolio our approaches are aligned to accelerate six of the 17 universal sustainable development goals (SDG's). These are good health and well-being, quality education, gender equality, industry innovation and infrastructure, reduced inequalities, responsible consumption and production.

Greenhouse gas emissions (GHGs) from the pharmaceutical industry (52 Mt CO_2 per annum) account for 20% of the total industrial carbon footprint. The UK pharmaceutical CO_2 footprint is 5.2Mt, around 70% of this stems from drug product manufacture (30% in distribution). This is growing rather than reducing and has the highest E factor amongst chemical using industries (up to 100kg of waste per kg of product). This is a consequence of the constrained timelines for development to meet the demands of clinical testing and safety, leading to suboptimal processes and reliance on waste disposal rather than avoidance. Through this strategy to digitalise CMC we will firmly enable reduced carbon emissions through Goals 9 & 12 (Industry, Innovation & Infrastructure and Responsible Consumption and Production).

* https://sdgs.un.org/#goal_section

5. Building on Academic Strengths

This strategy builds on and is informed by a portfolio of industry demand led manufacturing research in CMAC with academic strengths across a breadth of areas (Fig 1, below). CMAC's research portfolio (Fig 2) driven by a core academic team with the underpinning research expertise and capabilities to develop new integrated solutions across our medicines manufacturing scope.

ACADEMIC STRENGTHS

Next Generation Solid State
- Discovery and control of form (polymorphs, salts, solvates, co-crystals and amorphous)

Smart Crystallisation, Particle Engineering and Isolation
- Agile digital development for manufacturability, stability and performance

Smart Formulation and Drug Product Processing
- Agile digital development for OSD
- Material property database

Biorelevant Release and RTRT
- Quality by Digital Design (QbDD)
- Performance models
- Digital quality profile

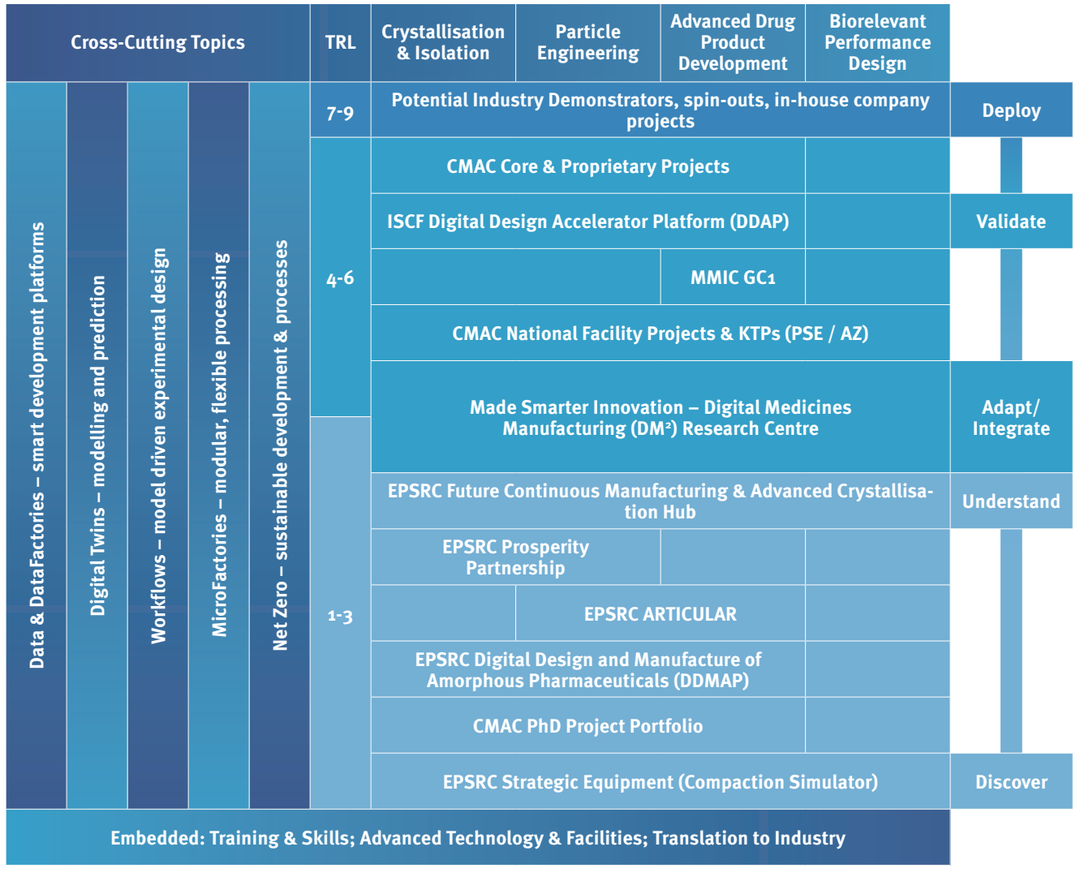
Advanced Characterisation
- Measurement methods across length scales
- Standards and data flows

Next Generation Digital
- Digitalised workflows
- Ontologies, data, databases and model libraries

MicroFactories
- Digital design for optimal performance
- Integrated Process Analytical Technology (PAT), control & operation for PoC

Skills
- Needs for Researcher of the Future
- MSc, PhD, CPD

Fig. 1. Activities led from world class facilities at the Technology & Innovation Centre at the University of Strathclyde also include leading translation to industry and skills development producing an industry-ready talent pipeline. Established in 2011, CMAC houses over 130 staff, researchers and students and a national and international network of academic and industrial partners.



ENABLING CAPABILITIES SUPPORTING CMAC PROGRAMS

Fig 2. (top) CMAC research platform areas, highlighting existing academic strengths and capabilities underpinning our research portfolio and that will enable us to deliver the integrated solutions and wider impacts from the 2021+ Strategic vision (bottom) enabling capabilities across our scope from API to Drug Product performance.

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.

Industry Partners and supporting organisations

University of Bath
University of Cambridge
University of Copenhagen
Ghent University
The Glasgow School of Art
The University of Nottingham — UNITED KINGDOM · CHINA · MALAYSIA
Imperial College London
University of Leeds
Loughborough University
The University Of Sheffield.
University of Strathclyde Glasgow
AstraZeneca
Chiesi
Lilly
Pfizer
Roche
Takeda
UCB
analytik
anatune — Collaborate · Innovate · Automate
AWL — Inspiring Innovation
blacktrace
Britest
CCDC — advancing structural science
CherryCircle
QbDVision
Clairet Scientific Limited
EDEM
gsk
Huxley Bertram
M-STAR Simulations
NiTech Solutions
Perceptive Engineering — an Applied Materials company
pwc
Siemens
Snapdragon Chemistry
Technobis — crystallization systems
ThermoFisher Scientific
connected everything.
cpi
Cancer Research UK
diamond
ICECUBES
MHRA — Regulating Medicines and Medical Devices
MMIP
NPL — National Physical Laboratory
Scottish Enterprise

Co-creation & Co-delivery

Our unique international network of academic and industry members, collaborators and supporters inform our centre's activities. We value our partners and focus on adopting ways of working that ensure colleagues are involved in the most relevant opportunities to identify new projects through an open, inclusive approach to co-creation. We ensure opportunities for impact are maximised via co-delivery and active participation at all stages. A summary of outputs from recent roadmapping events with Tier 1 partners is shown below (Fig 3).

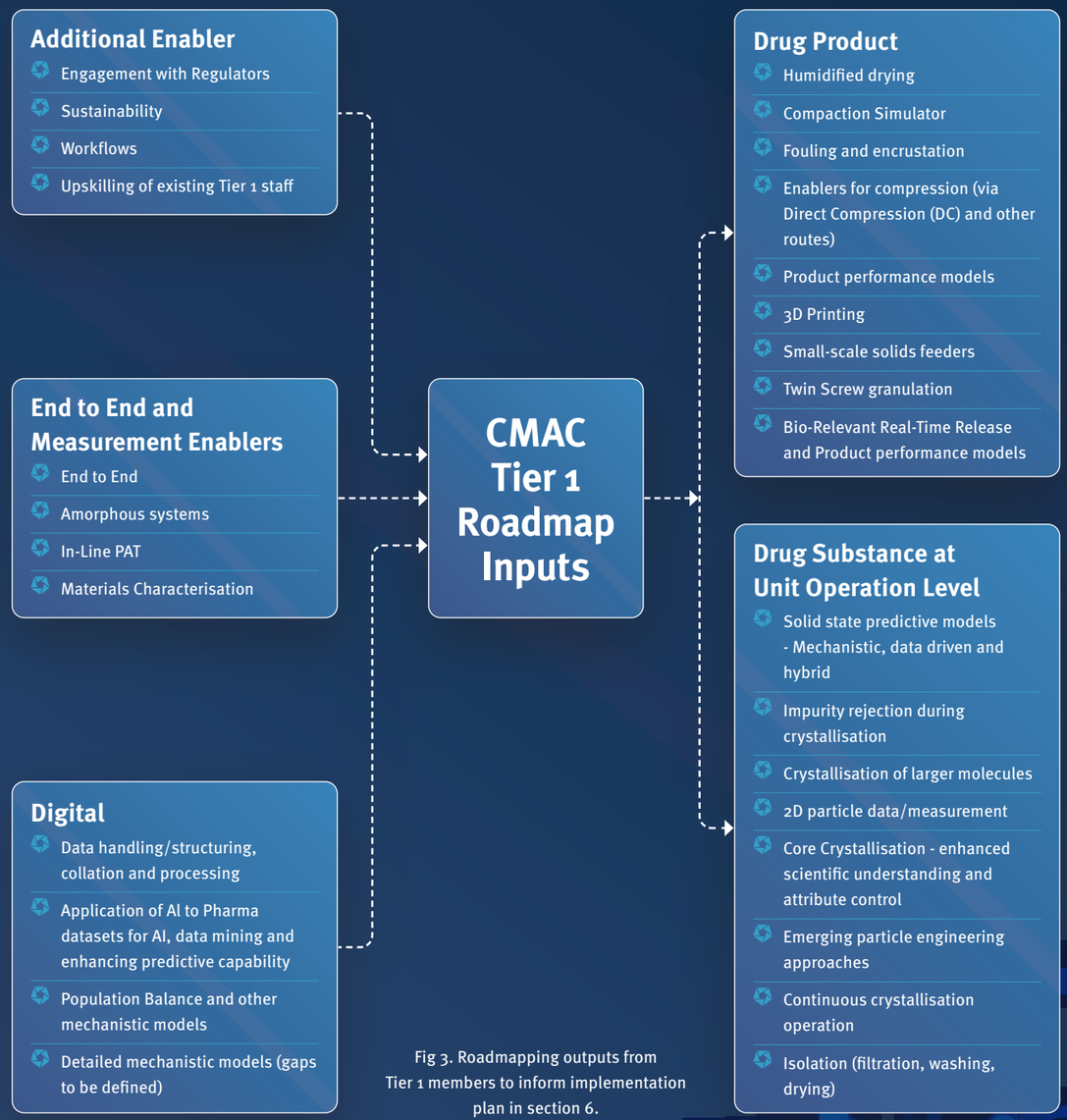


Fig 3. Roadmapping outputs from Tier 1 members to inform implementation plan in section 6.

External Environment

Our aim is to continue to strengthen the research base and its connection across the medicines manufacturing research and innovation ecosystem.

Our 2021+ Strategic delivery plan builds on collaborations across the community to grow medicines manufacturing and accelerate the adoption of advanced manufacturing and digital technologies.

To achieve this we propose an integrated approach, harnessing the combined efforts of partners and key stakeholders to lead the transformation that will enhance quality, cost and sustainability of medicines manufacture, ultimately for the benefit of patients. Working with academic partners, Tier 1 and Tier 2 industry partners, the regulators, MMIC and other innovation partners, CMAC will support the following sector objectives:

Regulatory:

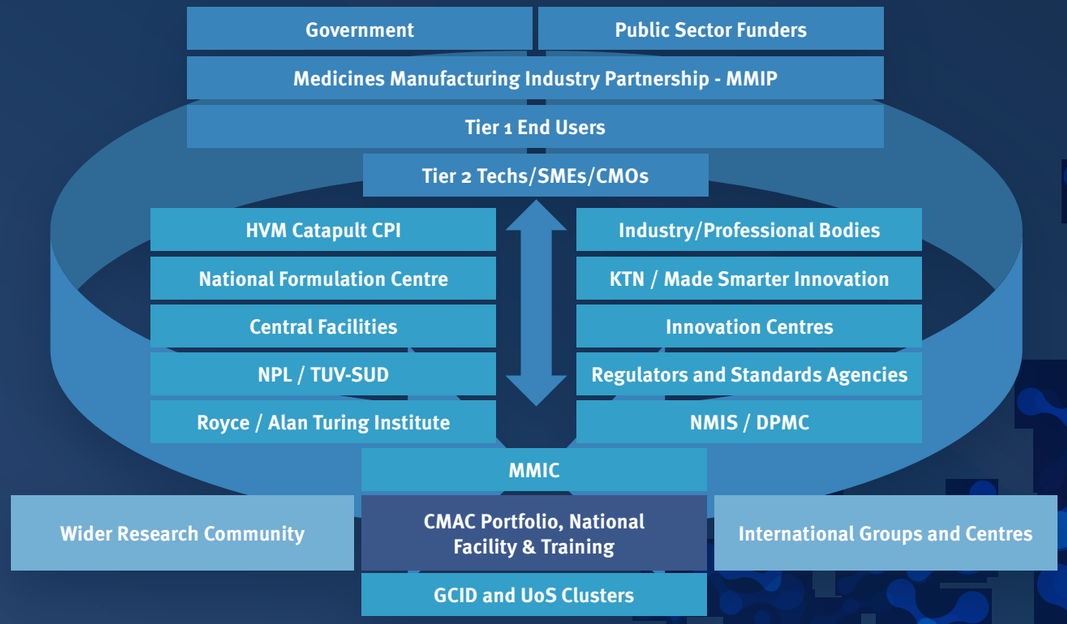
Protect and improve public health by enabling the earliest access and high-quality supply of safe, effective, and innovative products through proportionate, data-driven decisions on risk and benefits

Industry:

Leveraging the combined UK Innovation Ecosystem to deliver a more agile, adaptable and scalable medicine manufacturing supply chain

Academia:

Benefit from strategic commitment to support the world class research and innovation base for advanced manufacturing, digitalisation and sustainabilty. Secure support to continue to deliver and grow the industry-ready, highly skilled talent pipeline and to invest in new technology



Policy Alignment

In the UK, the Medicines Manufacturing Industry Partnership (MMIP) has a mission to support the UK to become a leading force in manufacturing innovation, to maximise Return Of Investment (ROI) from the exceptional UK R&D base, to be the leading force in manufacturing innovation, ensuring national and regional economic benefits and a secure supply of medicines for patients in the UK.

A Digital Transformation Agenda for Pharma: Digitalisation of medicines manufacturing is a key element of the MMIP strategy and is also highlighted in ABPI's Manufacturing Vision for UK Pharma and FDAs for global pharma. The Made Smarter report estimated £22.4Bn of value in the pharmaceuticals industry from adoption of IDTs to deliver digitally enabled R&D, manufacturing and supply, highlighting benefits from reduced cost, environmental impact and improved health. Given the strategic imperatives to achieve greater speed, quality, agility, security and sustainability, there is need for advanced pharmaceutical manufacturing, analytics and IDT development. The UK has supported a pipeline of industrial research programmes: ADDoPT, REMEDIES, ISCF Digital Design Accelerator Platform (DDAP) and the new Medicines Manufacturing Innovation Centre (MMIC). EPSRC has supported demand-led academic manufacturing research including the Future Continuous Manufacturing and Advanced Crystallisation (CMAC) Hub; Virtual Formulation Laboratory, ARTICULAR (AI in development) and others. DM2 co-created collaborative approach will go beyond these projects and build an integrated suite of innovative digital research Platforms that will accelerate the development and adoption of IDTs in MM.

Digital Transformation and Data-Driven Research Focus: The lifeblood of data-intensive science is to enable knowledge discovery by ensuring users and machines can discover, access, integrate and analyse task-appropriate data and associated metadata or models. Strong data foundations are crucial and we will lead the sector by implementing good data management policies and FAIR principles (findable, accessible, interoperable and reusable). To maximise benefit, our approach will embed regulatory data integrity guidance and needs (e.g. FDA 21 CFR Part 11; ALCOA+).

Influencing the Advanced Manufacturing and Digital Ecosystem

Acting as an International Research Centre, Driving Collaboration

White Papers

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

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

113 PhD students

36 Industry Placements since 2017

41 Industrial Mentors involved

Ongoing: PDRA development; External CPD

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

CMAC INDUSTRY BOARD

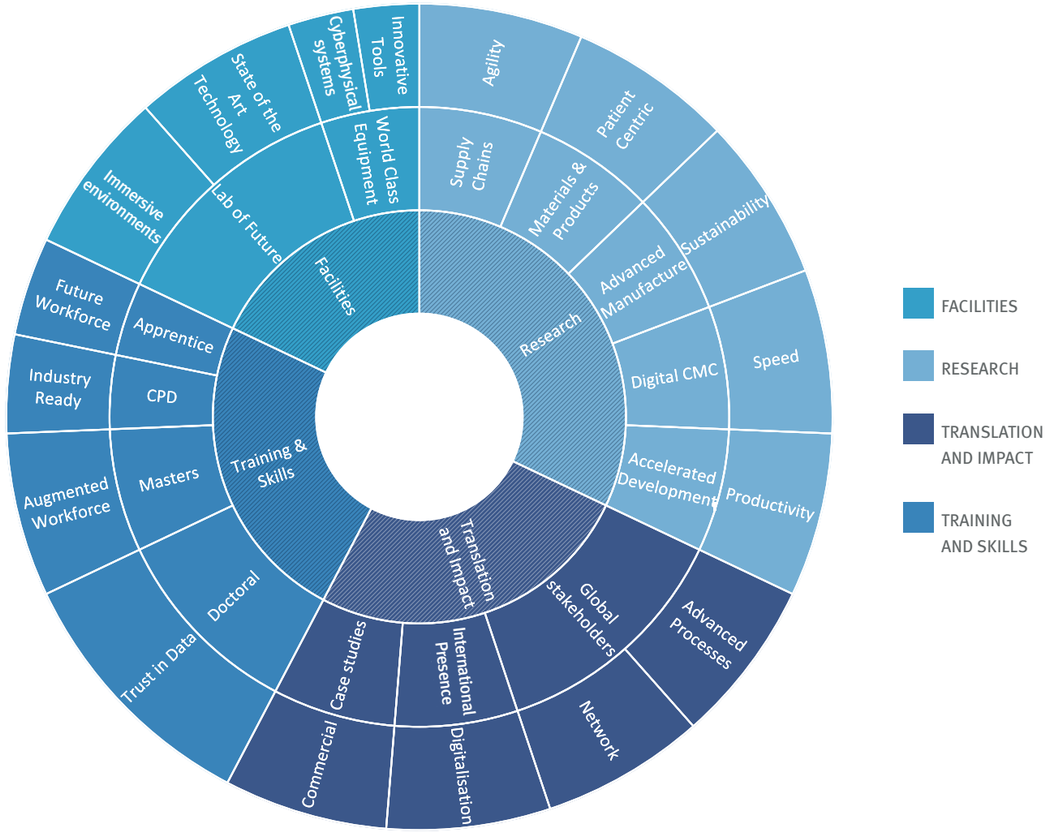
- Creating impact from research and application of data and digital technologies.
- Input and influence of policy through shaping of roadmaps for digital design, robotics & automation.
- Shaping the Skills agenda for the workforce of tomorrow.
- Creating infrastructure for the 'Lab of the Future'

6. 2021-26 Strategic Plan

CMAC's 2021+ Strategy will be delivered through our continued focus on CMAC's four core pillars that underpin all that we do.

Research Excellence & Intensity | **Outstanding Skills Development** | **World Class Facilities** | **Exemplary Translation to Industry**

We will continue to develop and grow our program across each of the pillars in areas co-developed with our partners that align to address industry needs. The figure below highlights some examples of key areas of interest.



PILLAR 1

6.1. 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)

Further details on each of these target systems are summarised in the Table below and in Fig 4.

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	• Probabilistic predictions on how molecular structure impacts particle formation • AI/ML tools integrated to inform process selection and design	• 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	• Model driven identification of CMAs, CPPs & CQAs • Product and process understanding • global sensitivity for integrated processes • Develop commercial digital solutions ready for industrial application & NDA submission
Benefits	• Support rapid translation • Inform screening & form selection • Data driven, mechanistic and hybrid predictive tools for: solvent selection, rapid estimation of crystallisation model kinetic parameters; impurity rejection; in silico process design • In silico process and particle design tools	• Enable decision tool for drug substance processes from process dynamics (batch vs continuous manufacturing) • MicroFactory selection system • Digital process and product design tools	• Develop digital release/digital quality control • Correlate dose, solubility and permeability on oral bioavailability • Effect of biorelevant dissolution • Improved in vitro prediction of in vivo performance	• Digital design space and operating ranges • Digital feasibility testing • In silico conceptual prototypes • Develop digital release / digital quality control • Implementation of QbDD

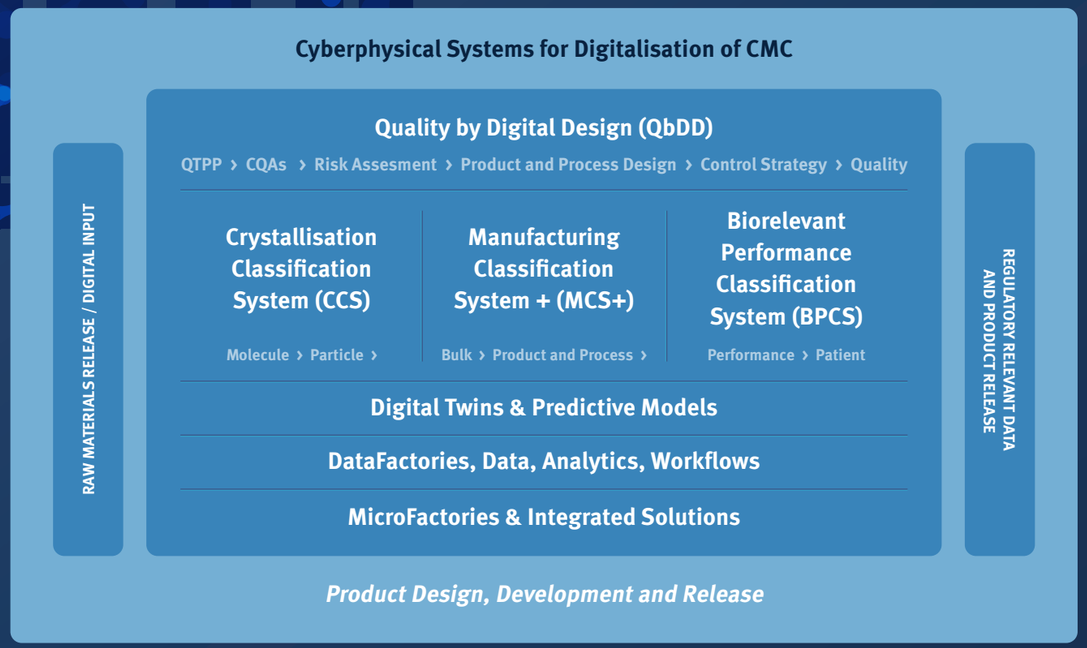


Fig 4. 2021+ Research Direction: Building Integrated Solutions to transform development and manufacture of medicines. Combining the academic expertise across our platforms and enabling capabilities to deliver an integrated platform for QbDD as a framework for digitalisation of CMC.

CMAC DataFactory - Autonomous AI and collaborative robotics enabled development platforms

Themes and Research Direction

We will deliver a rapid innovation pipeline of end to end flexible and sustainable continuous and modular manufacturing processes informed by leading edge digital design and exploiting industrial digital technologies. Key developments of the approach include:

- **DataFactories -** autonomous experimental DataFactory platforms capable of collecting targeted experimental data for APIs, excipient and products under a wide range of conditions exploiting automated dosing or sample handling, mobile robotics, small-scale experiments with integrated sensing/analytics/image analysis for information extraction and global optimisation for self-learning experimental planning to meet objectives.
- **Digital Twins (DT) -** integrated digital framework to collate, analyse, visualise and apply data, models and knowledge of the rapid design, control, operation and testing of continuous and modular processes for API crystallisation and DP production. The DT will combine the overarching digital definition of the materials, products, equipment and processes. We will use the QbDD workflows to gather data and inform model development, optimisation and implementation; these data, models and metadata will then be captured, stored and interrogated in the DT framework to drive process design and operation. Process DT will inform supply chain modelling and design.
- **MicroFactories -** research MicroFactory test beds will run the processes defined in the DT. We will design and build MicroFactory platforms comprising integrated, modular unit operations with PAT and real time control. Unit operations will include (i) crystallisation and particle engineering for controlled particle attributes (e.g. size, shape, form, purity) from input stream of API + impurities + solvent(s); (ii) filtration, washing and drying to isolate dry powder with desired properties; (iii) integrated polymer processing of powder to product, DP, capsule filling, wet granulation, roller compaction and/or direct compression; (iv) other techniques for emerging applications e.g. spray drying, microfluidics for LNP production.
- **Workflows -** The QbDD Workflow will drive experimental efforts within DataFactories, to populate the QbDD Digital Twin and enable transfer of process designs and control strategies into operation in appropriate MicroFactory test beds. We will model and predict material, product and process outcomes using optimal experiments and measurements driven by model requirements.

Benefits of Advanced Manufacturing and Digitalisation of CMC

Advanced DataFactory and MicroFactory process technologies coupled with QbDD workflows, Digital Twins and our new predictive tools (CCS, MCS+ and BPCS) will deliver the Digitalisation of CMC. This will allow us to realise an integrated, Cyberphysical system for development and manufacture of medicines that will:

- Enable us to identify and understand all the critical quality attributes of products
- Establish a virtual process model, for all of our processes, paired with product models – creating an integrated digital design space
- Combine development and manufacturing data to validate and strengthen the models
- Exploit these validated models to inform control strategy and control manufacturing processes and ensuring models continue to adapt and learn
- Enable digital QC to control the quality of products automatically and the processes are optimised continuously, dynamically and autonomously
- Create new business models and supply chains for patient centric agile and secure supply to benefit healthcare providers and patients

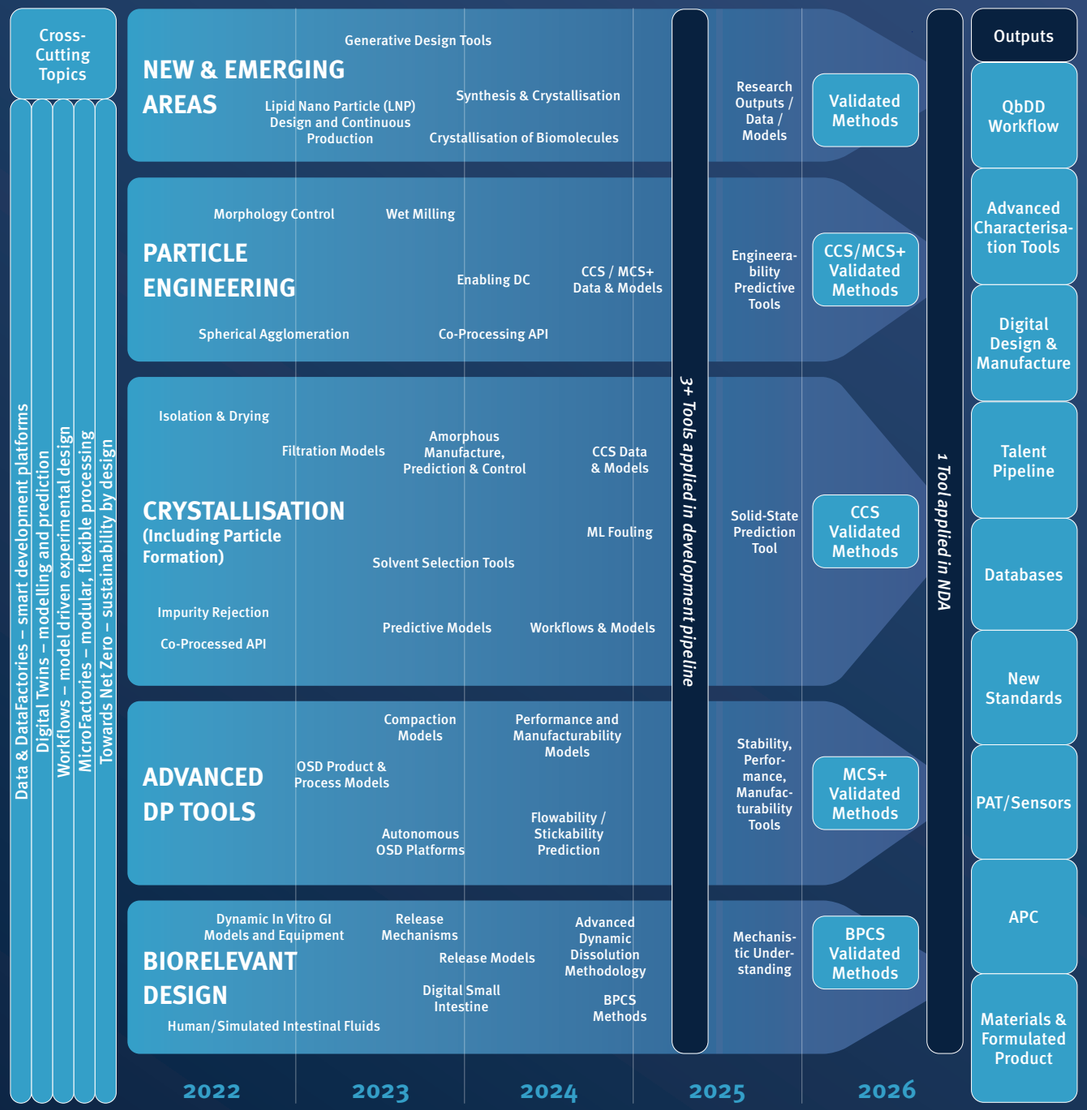
Research Value Chain

Strategic Statement of Intent:	**Create value to partners from a co-created, high quality research portfolio across advanced manufacturing, digital technologies, materials science to enable QbDD and digitalised CMC processes**
Timeline:	2022 | 2023 | 2024 | 2025 | 2026
Objectives:	Target areas → Co-deliver solutions → Assess research tools → Drive acceptance & adoption → Tools in practice
Activities:	Implement strategic roadmap priorities | Collaborative research delivery | Disseminate outputs + integrated toolbox informing new projects | Target remaining gaps in roadmap | Sustain work & community
Deliverables:	Co-created research proposals in priority areas + Formulate Hub-follow on plan | DataFactory; MicroFactory; Digital Twin ex Hub & DM2 + EPSRC critical mass post 2023 + 1st versions of CCS; MCS+ | Demonstration of research tools from portfolio in Tier 1 development pipelines + BPCS development | Integrated toolbox of CCS; MCS+, BPCS enabling QbDD | Digitalised CMC process implemented in NDA
Impacts:	Managed portfolio of collaborative research | CMAC Tier 1/2s actively engaged in research + new tools developed | Research impacting Tier 1 internal development pipeline | Speed, material sparing, sustainability and quality objectives validated | IDTs and Advanced Technologies implemented across Tier 1s

Research Implementation Plan

To achieve our vision, key objectives have been highlighted through our mission which will be delivered through our four pillars enabling work on our new strategic goal of delivering a QbDD workflow.

We have mapped out with our partners the priorities for 2021+ plus building on the portfolio below and identifying new project activities across the portfolio to address the key areas in each of our strategic research themes. New and emerging areas; particle engineering; crystallisation and particle formation; advanced drug product tools and biorelevant design.



PILLAR 2

6.2. Outstanding Skills and Development

CMAC has a leading training programme recognised for uniquely serving the MM sector talent pipeline. The lack of appropriate skills in the workplace is identified as the main barrier for translation and adoption of disruptive, innovative advanced and digital MM technologies. The Centre will continue to deliver the long-term skills needs to enable the workforce of tomorrow aligned with our research and translation strategy from our world-class facilities through:

1. Industry PhD programme
2. MSc in Advanced Pharmaceutical Technologies + more
3. CPD and transferable skills for staff and students
4. CPD for upskilling partner staff, aligned with translation of our Industrial Digital Technologies

We will deliver this by:

Strategic Statement of Intent:	Create Societal & Cultural Change by enabling an augmented workforce of people with broader skills and more diverse teams to drive innovation, productivity and sustainability in medicines development & manufacturing				
Timeline:	2022	2023	2024	2025	2026
Objectives:	Identify need	Co-create solutions	Drive acceptance & adoption	Sustained cohorts	Skills in practice
Activities:	ID research challenges & training needs + funding case	Implement best practice	Disseminate outputs & impacts	Ongoing training + recruitment + review	Sustain work & community
Deliverables:	Knowledge & skills gaps for advanced manufacturing training + PhD cohort recruitment	Online training platform from DM2 established + refreshed curricula + new research outputs	Demonstration of training addressing gaps identified + placements	Maintain curricula at appropriate levels + placements + CMAC talent pipeline at 150 students delivered	Excellent training experience in advanced medicines manufacturing
Impacts:	CMAC training forum including masters, PhD, ECR and CPD needs	CMAC Tier 1/2 community engaged in training and continued education	Created community forum & foundations for skills academy	Recruitment into Tier 1s, leading academia, regulators, Tier 2s	>100 high value jobs supported and created across medicines manufacturing

"The demand for multidisciplinary talent is uniquely served by CMAC"

CMAC INDUSTRY PARTNERS

- World-class training programme uniquely placed to address the interdisciplinary challenges in pharmaceutical manufacturing
- Delivering the next generation of highly skilled researchers and future workforce that will drive the transformation of advanced pharmaceutical manufacturing

PILLAR 3

6.3. World Class Facilities

CMAC has attracted substantial co-investment in recent years from EPSRC, UK-RPIF, industry, SFC, Wolfson Foundation and others to establish a comprehensive suite of equipment and instrumentation to support our research, training and translation agenda. Located within a bespoke suite of over 900m² of laboratory space within the Technology & Innovation Centre (TIC) at Strathclyde, CMAC's National Facility offers unique access to a comprehensive array of medicines manufacturing research and training capabilities.

In addition to an extensive range of small-scale batch and modular continuous primary processing and particle engineering technologies, PAT, automation and control capabilities, we have a wide range of secondary processing, materials characterisation and testing platforms to support collaborative research teams. We have invested in a range of digital technologies for data acquisition, sharing, modelling, simulation and visualisation. Our suite of analytical laboratories provide advanced understanding of particulate formation and processing, and a secondary processing suite. In addition to supporting research and training activities, there is a dedicated, specialised support team within CMAC to offer services and assistance to academic and industry partners across our scope.

The University of Strathclyde is expanding its presence within the Glasgow City Innovation District (GCID) with new TIC buildings expanding the current TIC footprint. As part of this strategic growth CMAC will be expanding our laboratory and office footprint to support our 2026 vision. With enhanced facilities and further capital investment in innovative technologies embedding Industry 4.0 principles and industrial digital technologies on our research infrastructure we will establish a beacon of best practice. This CMAC Lab of the Future concept will support growth across our programme, enable dedicated training programmes in advanced manufacturing and accelerate digitalisation of pharmaceutical development and manufacturing research.

Facilities Value Chain

Strategic Statement of Intent:	Deliver a world leading Lab of The Future by embedding innovation, integrated tools & high standards in CMAC's infrastructure to support high quality collaboration across research, training and skills and translation to industry.				
Timeline:	2022	2023	2024	2025	2026
Objectives:	Identify needs	Planning & implementation	Drive acceptance & adoption	CMAC Lab of Future	Next generation tools routine
Activities:	Finalise targets and develop funding plan	Active rolling replacement and upgrade program	Integration of IDTs & advanced process technology	New tools from portfolio + technology development	Digital CMC platform and QbDD tools
Deliverables:	Defined CMAC GCID-TIC footprint; prioritised CAPEX objectives informing funding plan	Datafactory; MicroFactory and Digital Twin capabilities in place for demonstration + Digital Twins, ML/AI, VR/AR, robotics tools	Integrated framework connecting data, modelling, processing and performance + dedicated test bed labs + containment	Integrated digital CMC platform [DataFactory; MicroFactory and Digital Twin across portfolio supporting CCS; MCS+; BPCS and QbDD]	New methods, standards, showcase, use cases and business case validated
Impacts:	State of art technology base; integration of digital toolbox	First CMAC Lab of Future test beds showcasing technologies	Acceleration of use and development of advanced technology +	Industry 4.0 ways of working supported for researchers and Tier 1 partners	Transformation of lab infrastructure + access to innovative tools

CMAC Lab of Future, integrating advanced technologies and digital solutions within medicines manufacture R&D and skills development.

PILLAR 4

6.4. Exemplary Translation to Industry

Deliver value to partners through supporting a managed programme of translation of CMAC assets to higher TRL to translation to industry design phase achieve targeted improvements in Tier 1 capabilities across scope of research portfolio.

Translation to industry is a core mission for most UK and international academic innovation centres and exemplary translation to industry has been a hallmark of CMAC from its inception. As CMAC enters its second decade, there is a renewed sense of urgency to accelerate translation activity to meet the demands of an ever-accelerating world of change in which its industry partners compete.

Our aim is to achieve an elevated level of awareness of the benefits and opportunities for key stakeholders, and to implement via co-creation, co-delivery, dissemination, training and discovery of translation routes. The will disseminate to a higher TRL towards commercialisation and industrial application of innovative solutions.

CMAC's translation to industry programme of activities offers a variety of routes to translation as well as our relationship with MMIC, and 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, join the partnership and help accelerate the adoption of advanced pharmaceutical manufacturing.

Multiple routes of translation to industry (T2I)

How

TRL based development and progression
- T2I via strategic partnerships. CPI/ MMIC)
- T21 in collaboration with Tier 1 and/ or tier 2
- Commercialisation via CMAC NF

Staff Exchanges
- PhD Placements at companies
- Company Staff at CMAC

Recruitment

Collaboration
- Proprietary 1:1 project collaborations
- Pre-competitive industry funded programs

Training
- Webinars and E-learning modules
- At company sites, or at CMAC

Portfolio

TRL 1 to 3

TRL 3 to 6

Active in T2I phase
- Digital Platforms
- Predictive Models & Software
- Workflow/S
- Data Base & Know How
- Hardware & New Sensors
- Materials Characterisation
- Skills Development

Current figures to date

CMAC Tech Portfolio (>=3)

22 technologies in total:
- 6 are TRL 3
- 11 are TRL 4
- 4 are TRL 5 Tidesign ph
- 1 T2i active via MMIC
- 1 commercial readiness

Several conceptual technologies at TRL 1- 3 currently progressing within the CMAC Research and Translation Portfolio

The critical mass of scientific operations, academic leadership, expertise, focus on accelerating adoption and delivering impact from our research has enabled CMAC to develop a portfolio of technologies that have now reached TRL 3-6 and continuing develop a suite of new technologies and capabilities at TRL 1-3 informed by the challenges and emerging needs of industry.

CMAC has instituted a stage-gate process as a means of managing technologies from lower TRL to higher TRL. The purpose is to achieve a go/no-go decision on further resource investment in a technology concept.

At the first phase, a review is done with the research team to determine any disruptive or innovative capabilities of the technology, preliminary identification of industry-specific customer jobs addressed, and determine the fidelity and usability of the technology, as well as detecting barriers and risks to adoption. IP strategy options at this point are contemplated and defined.

Translation to Industry Internal Decision Gates

CMAC Research & Translation Portfolio

IP strategy
- If no IP/patent, then publish and expand work as relevant reputationally

Monetisable?
- If yes, seek out commercialisation partners
- If no, seek to maximize translation to industry

Academic community incentive
- IP, support to commercialise, funding, reputation, open innovation

End-user incentive
- Enhance technology capability/ competitiveness, cost saving, risk reduction/sharing, financial gain

Review with Research Team

Determine disruptive/ innovative capabilities

Identify industry-specific customer jobs addressed

Determine fidelity, usability, technology barriers/risks

Critical Decision 1: Technology value proposition (TRL 3)
- Determine IP & strategy
- Monetisation strategy/ TAM
- Customer segments/ likely partners
- Resources needed to progress technology development
- Go/no-go decision

Engage with Tier 1 End-users

Determine technology risk & readiness

Determine technology future state URS/ development trajectory

Determine barriers to adoption/ market entry

Critical Decision 2: Technology Investment decision (TRL 5)
- IP protection
- Identify translation-to-industry partners/ strategy
- Value capture/business model/market research
- Financial plan/resource requirements to deliver
- Go/no-go decision

Objective: Achieve a go/no-go decision for further resource investments in a technology.

Translation to Industry Vision integrated into CMAC Strategy

Strategic Statement of Intent:	To develop, translate and operate continuous and advanced manufacturing solutions for the Pharma industry to improve compliance, productivity, speed to market and carbon footprint performance				
Who:	CMAC	CMAC	CMAC/T2I	T2I partner/s	T2I partner/s
Roadmap:	Research/applied research TRL 1 to 4	Translation portfolio TRL 3 to 6	T2I ideation and value case	Benefits use at commercial cases TRL 5 to 9	Pivotal/GMP scale Tech operation MRL >6
How:	Funded projects active with all stakeholders engaged	Tools mapped to TRL & translation pathways	Translation portfolio growth	Review of industrial application & scale up	Industrial scale for tech and capacity – ready
Deliverables:	Acceleration of first wave of CMAC technology assets across early TRLs and Tier 1s	CMAC technology assets via IAA; KTP; core project; 1:1; MMIC or spin out	CMAC translation platform for physical, digital and skills assets + sustained development of CMAC/ MMIC projects	Cost, quality +/or sustainability benefits; industrial scale validation	Industrial operation and skills + commercial ROI
Impacts:	De-risked/accelerated research and innovation + skills	Prioritised translation of CMAC technology assets + new partners engaged	Increased number of processes and products in development benefiting from technologies	Application at industrial scale + GCID and MMIC opportunities maximised	Tech ops in place and industrial case validated

7. Centre Sustainability & Growth

CMAC Growth Planning

CMAC has developed an ambitious business case to drive the growth of the Centre over the next 5 years and deliver further benefits to our partners and stakeholders. The case identifies growth targets across each pillar to extend our portfolio and enhance the scope, pace and impact of what we do. This will allow us to continue to develop our academic, technical and operational capacity as well as the vital infrastructure and equipment base to carry out research and provide staff and trainees with access to state-of-the-art technologies to support their research.

Staffing

We are moving forward with progressive recruitment plans that augment our operational and research core. Current plans aim to recruit over 30 new staff to support our core functions, partner engagement and build capacity and capability for the national facility team, supporting the delivery of our strategy. In addition, we are launching a recruitment drive for new academic positions located within CMAC.

Internationalisation

With University support we are carrying out a feasibility study on internationalisation of CMAC. Our aim is to support research growth; business growth; more effective collaboration with existing as well as new partners and improve access to and retention of international talent. The potential to contribute to CMAC sustainability and business resilience will also enable our partners to operate with us in a more geographically diversified way.

Facilities

CMAC's award winning facilities within the Technology & Innovation Centre (TIC) at the University of Strathclyde are located within the Glasgow City Innovation District (GCID) and provide a unique environment for interdisciplinary collaborative research. As part of the University's ongoing development of GCID and TIC, CMAC are developing plans to expand our laboratory footprint and enhance areas of infrastructure to support our Lab of the Future agenda. The planned CMAC Facility developments include extended space for research, dedicated training areas, enhanced containment, improved support for collaboration and integration of digital technologies.

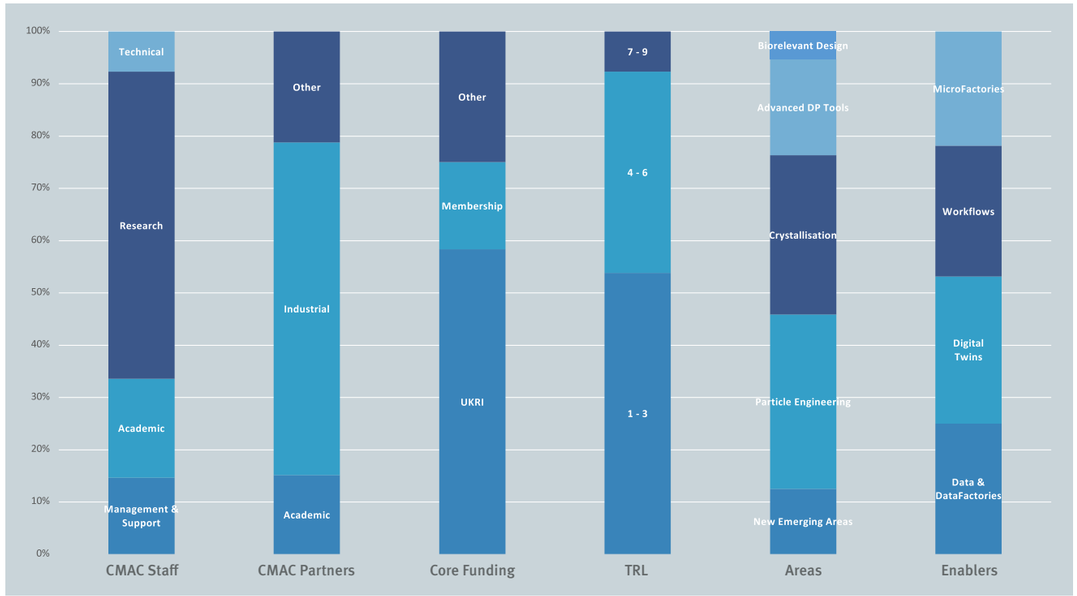
Funding

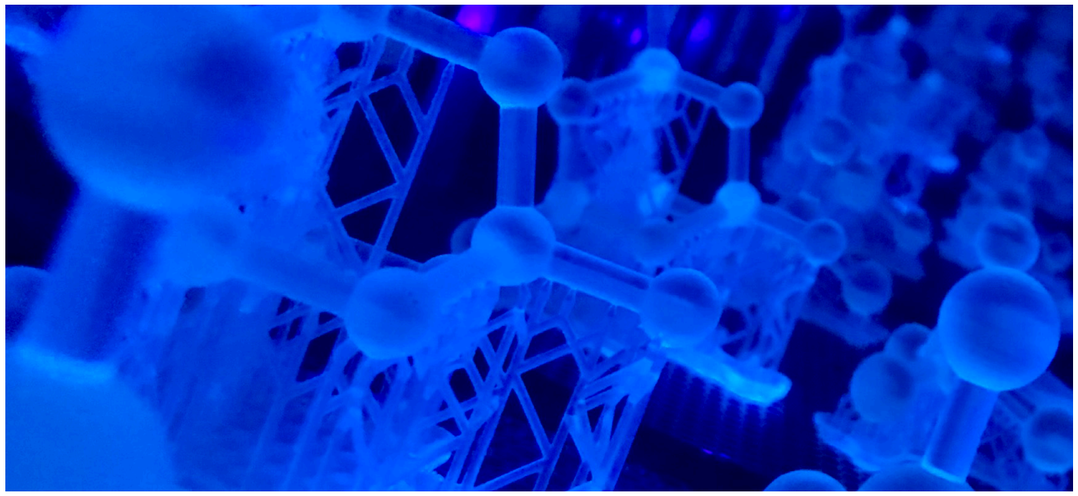
In support of our refreshed strategy and growth plans we will continue to identify priority areas to target additional funding efforts. Our dedicated Funding Manager will work closely with the Centre leadership, academic team and our partners to progress a pipeline of projects targeting priority needs. We seek to build a sustainable portfolio of demand led manufacturing research, skills, facilities and translational development.

8. Portfolio

Research Portfolio & Technical Scope @ 2021

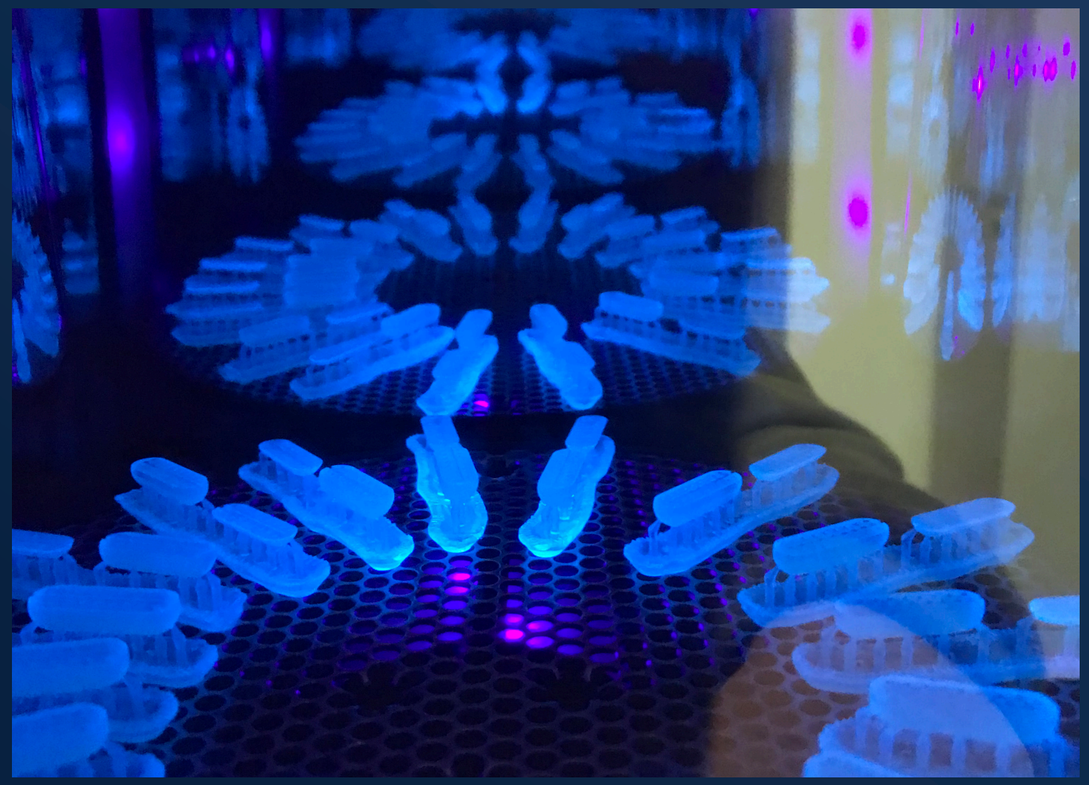
The entire CMAC research portfolio currently comprises over 80 projects. Our Tier 1 partner companies support collaborative research through the CMAC membership structure as well as proprietary projects, on a case by case basis. These are reviewed annually and the current shape of the Centre, programme partners and funding, TRL, topics and technologies are illustrated below.





9. Conclusion

Informed by our industry partners needs and aspirations we have together co-developed a unique and ambitious strategy presented here. Together we are targeting: the development of new science informing advanced pharmaceutical materials, products and processes and the digitalisation of CMC activities using innovative, integrated digital solutions. This co-created vision will accelerate product and process design, enable advanced manufacturing across API and DP and support more agile, sustainable medicine supply chains. By continuing to work collaboratively across our research, training, facilities and translation goals we will address the major challenges facing medicines manufacturing and transform the way medicines are developed, manufactured and supplied to meet the needs of patients.



Centre Management Team

Name	Position
Prof Alastair J. Florence	Director: alastair.florence@strath.ac.uk
Massimo Bresciani	Industry Director: massimo.bresciani@strath.ac.uk
Dr Andrea Johnston	Associate Director
Dr Mohammed Al Qaraghuli	Project Manager
Dr Rebecca Dean	Funding Manager
Helen Fielden	Project Manager
Dr Ian Houson	Technical Portfolio Manager
Dr Rhys Lloyd	Hub Impact Officer
Dr Thomas McGlone	Technical Operations and Tier 2 Manager
Dr Iyke Onyemelukwe	Translation and Tier 2 Manager
Dr Alison Robinson	Business Development and Key Account Manager
Dr Kenneth Smith	National Facility Technical Project Manager

Management Support Team

Name	Position
Subhaa Arumugam	Digital Developer
Lorna Gray	Centre Administrator
Dr Gillian Halket	Skills Coordinator
Morell Kerr	Directors' PA
Rebecca O'Hare	Assistant Centre Administrator
Rebekah Russell	Tier 1 Adminstrator

Strathclyde Academic Team

Name	Name
Prof Hannah Batchelor	Dr Alison Nordon
Dr Cameron Brown	Dr Iain Oswald
Dr Javier Cardona	Prof Yvonne Perrie
Prof Alastair J. Florence	Prof Chris Price
Prof Gavin Halbert	Dr John Robertson
Prof Blair Johnston	Prof Jan Sefcik
Dr Daniel Markl	

National Facility Team

Name	Position
Dr Christoph Busche	Physico-Chemical Analysis Team Lead
Dr Niki Hamilton	Process Technician
Dr Alan Martin	X-Ray Facility Instrument Scientist
Mark McGowan	Process Technician
Dr Aruna Prakash	Research Associate
Dr Humera Siddique	Senior Instrument Scientist
Mariam Siddique	Process Technician
Vishal Raval	Senior Continuous Processing & Analysis Engineer
Dr Alice Turner	Research Technician

For more information, also contact - info@cmac.ac.uk or see www.cmac.ac.uk

Tier 1 Partners contributing to this strategy document:

AstraZeneca Chiesi Lilly Pfizer Roche Takeda UCB

Academic Teams Supporting Portfolio

EPSRC Future Continuous Manufacturing and Advanced Crystallisation Research Hub

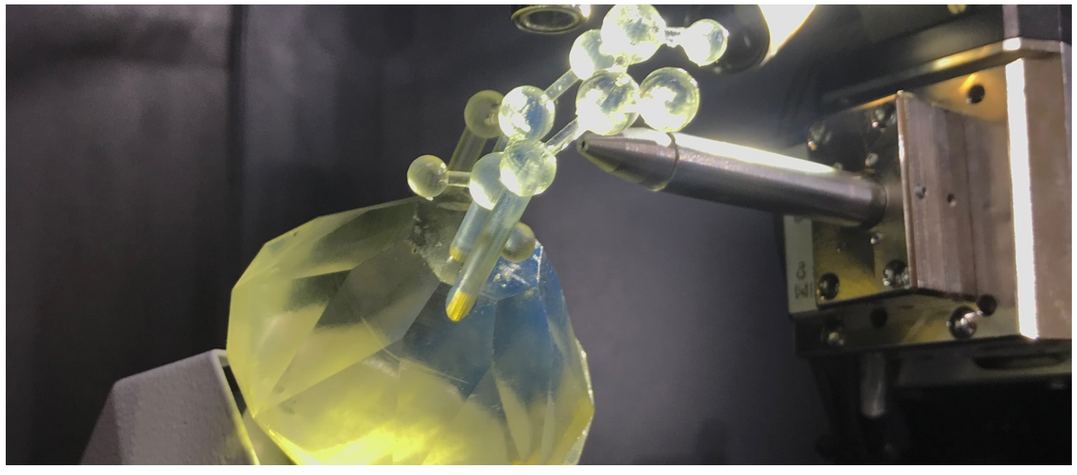
University	Name	
University of Strathclyde	Prof Alastair J. Florence Massimo Bresciani Dr Cameron Brown Prof Gavin Halbert Dr Andrea Johnston Prof Blair Johnston	Dr Daniel Markl Dr Alison Nordon Prof Chris Price Dr John Robertson Prof Jan Sefcik
Bath	Prof Chick Wilson	
Cambridge	Dr Jagjit Srai	
Imperial College London	Prof Claire Adjiman Prof Amparo Galindo	Prof George Jackson
Leeds	Prof Sven Schroeder	Prof Kevin Roberts
Loughborough	Prof Chris Rielly	Dr Brahim Benyahia
Sheffield	Prof Jim Litster	Dr Rachel Smith

EPSRC ARTICULAR

University	Name
Strathclyde	Prof Blair Johnston Dr Cameron Brown Prof Alastair J. Florence
Loughborough	Dr Brahim Benyahia Prof Chris Rielly
Glasgow School of Art	Prof Paul Chapman Dr Steve Love

Made Smarter Innovation - Digital Medicines Manufacturing Research Centre (DM2)

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



Projects

Innovate UK Digital Design Accelerator Platform, DDAP

University	Name
University of Strathclyde	Prof Alastair J. Florence Dr Cameron Brown Dr Andrea Johnston Prof Blair Johnston

EPSRC International Centre to Centre, Digital Design and Manufacture of Amorphous Pharmaceuticals, DDMAP

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

Innovate UK Knowledge Transfer Partnership with PSE

University	Name
Strathclyde	Prof Alastair J. Florence Dr Cameron Brown
PSE	Dr Niall Mitchell

Innovate UK Knowledge Transfer Partnership with AZ

University	Name
Strathclyde	Prof Alastair J. Florence Prof Blair Johnston
AstraZeneca	Dr Helen Blade Dr Amy Robertson

MMIC Grand Challenge 1

University	Name
Strathclyde	Dr Daniel Markl Dr John Robertson

AMCF ERDF SCOUT (Scottish Outreach)

Partners	Name
CPI CMAC IBioIC	Dr Rebecca Dean Rebecca O'Hare Dr Kenneth Smith

EPSRC RiFTMaP, Right First Time Manufacture of Pharmaceuticals

University	Name
Sheffield	Prof Jim Litster Prof Daniel Coca Prof Mahdi Mahfouf Prof Agba Salman
Strathclyde	Prof Blair Johnston Dr Daniel Markl
Purdue	Prof Gintaras Reklaitis Prof Marcial Gonzalez Prof Zoltan Nagy
UCL	Prof Ian Bogle Prof Vasileios Charitopoulos

Prosperity Partnership Theme 4 with GSK

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

Community for Analytical Measurement Science (CAMS) funded Understanding long- term stability of solid pharmaceutical dosage forms

University	Name
Strathclyde	Dr Daniel Markl Dr Ibrahim Khadra
Partners	AZ, Pfizer

EPSRC SolvIT; Computer aided solvent design to minimise solvent use in integrated synthesis, purification & isolation for sustainable

University	Name
Strathclyde	Dr Chris Price Prof Jan Sefcik Dr Jun Li Prof Billy Kerr Dr David Lindsay Dr Sara Ottoboni
Imperial College London	Prof Claire Adjiman Prof Amparo Galindo Prof George Jackson

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