Advancing Sustainability in Pharma Sector

UK / India NetZero Innovation Centre : Decarbonisation of Indian Pharmaceuticals, Fine & Specialty Chemicals Industries

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Department for Science, Innovation & Technology

सत्यमेव जयते
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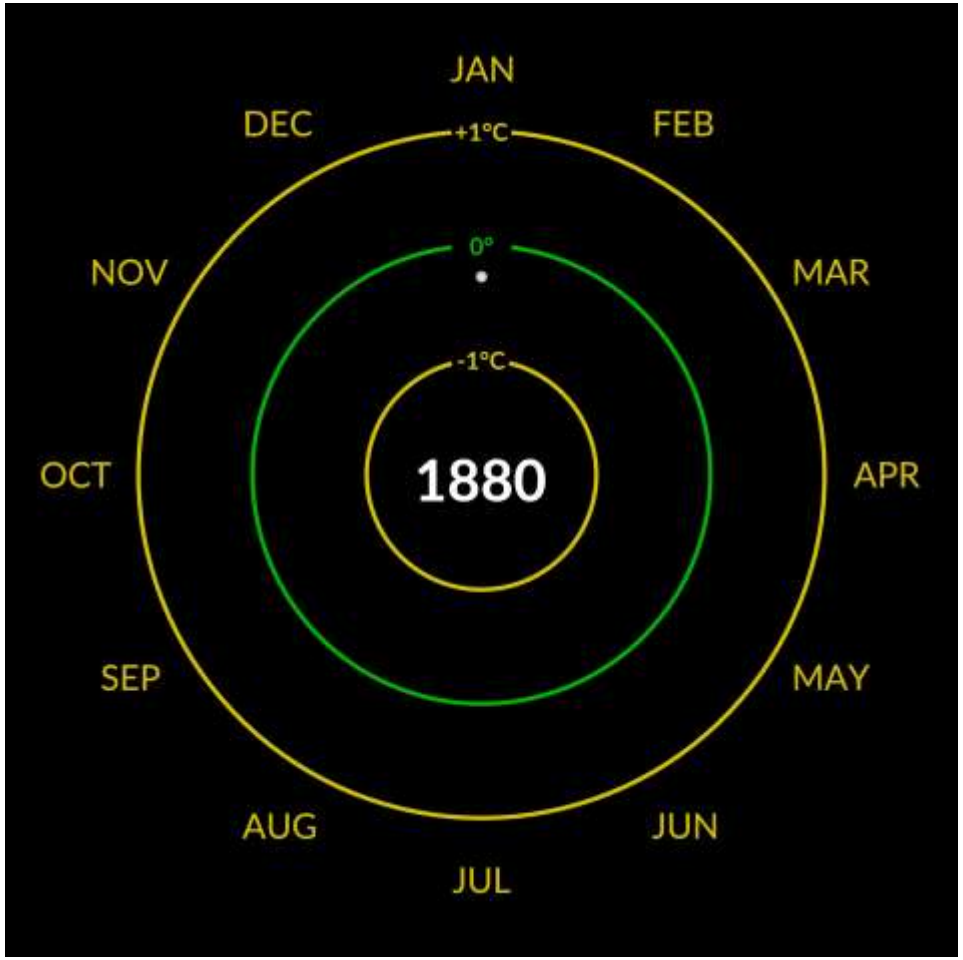
The Environmental Challenge

Impact of Greenhouse Gases on our Planet



NASA's Scientific Visualization Studio

Global Warming Headlines

More Droughts and Heat Waves
Periods of abnormally hot weather lasting days to weeks are projected to become more intense, and cold waves less intense and less frequent

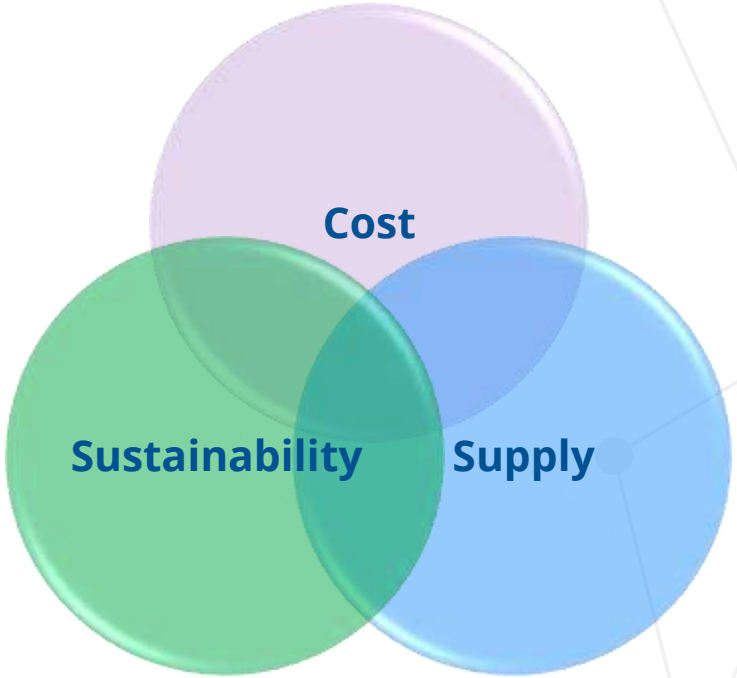
Global sea level has risen about 20cm
Since reliable record-keeping began in 1880 and by 2100 it will rise another 30cm but possibly as high as 2 meters.

Changes in Precipitation Patterns
Climate change is having an uneven effect on precipitation, with some locations experiencing increased precipitation and flooding, while others suffer from drought.

Hurricanes have become Stronger and More Intense
Associated storm intensity and rainfall rates will continue to increase as the climate continues to warm.

The challenge

- In 2023, the Indian chemical industry contributed 7% to GDP and emitted about 57 Mt CO_2.
- Indian Pharma and Fine & Specialty Chemicals sector contributed nearly
  30% of this emission.
- The Global Pharma Sector has a larger carbon footprint than the Automotive industry
- The World order is more dynamic than it has been in several decades



Industry macroeconomic trends and drivers

Political, Governmental

Drivers

- Global Environmental Forums (COP)
- Target
- Regulators

Implications

- Statutes, Standards, Protocols
- Restrictions (CFCs)
- Tariffs, Penalties, Fines

Commercial & Societal

Drivers

Expectations of

- Payers
- Consumers
- Next Generation

Implications

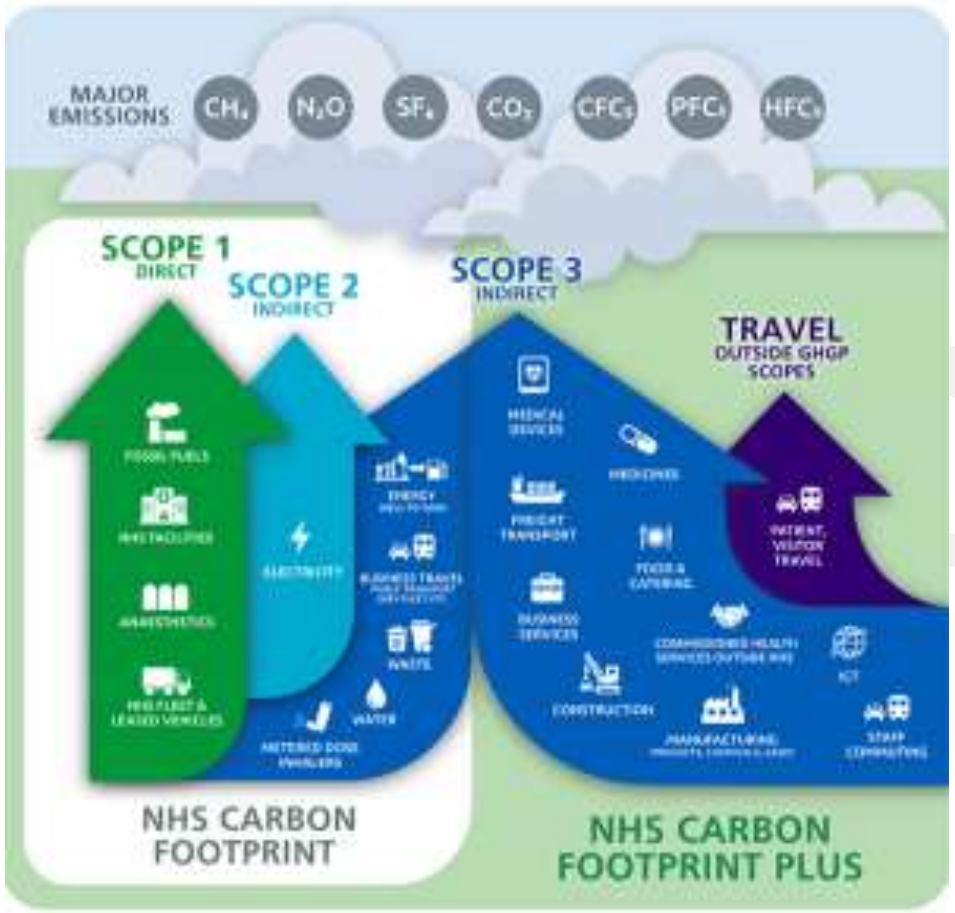
- Buyer behaviour
- Market Choice
- Public conscience and expectations

Goals & Targets

National Health Service (NHS)

As the biggest employer in the country responsible for 4 per cent of England's total carbon emissions, there are many diverse opportunities to make inroads.

- **Net zero by 2040 for the NHS Carbon Footprint,** *(with 80% reduction by 2028 to 2032)*
- **Net zero by 2045 for the NHS Carbon Footprint 'Plus',** *(with an ambition for an 80% reduction by 2036 to 2039.)*



The Greener NHS report, Delivering a Net Zero Health Service, collates examples of what can and should be done to achieve the aim, including:

- working with pharmaceutical companies to reduce emissions from high-carbon medicines such as inhalers and anaesthetic gases.

Where Next?

https://www.europarl.europa.eu/RegData/etudes/STUD/2023/747453/EPRS_STU(2023)747453_EN.pdf

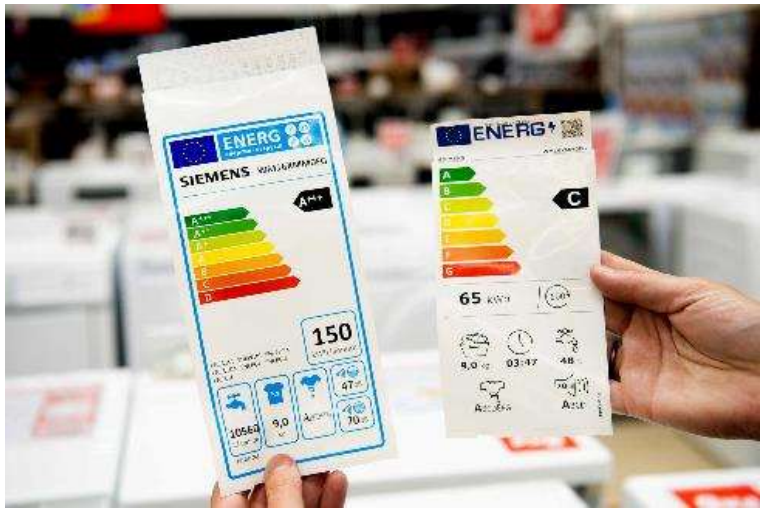
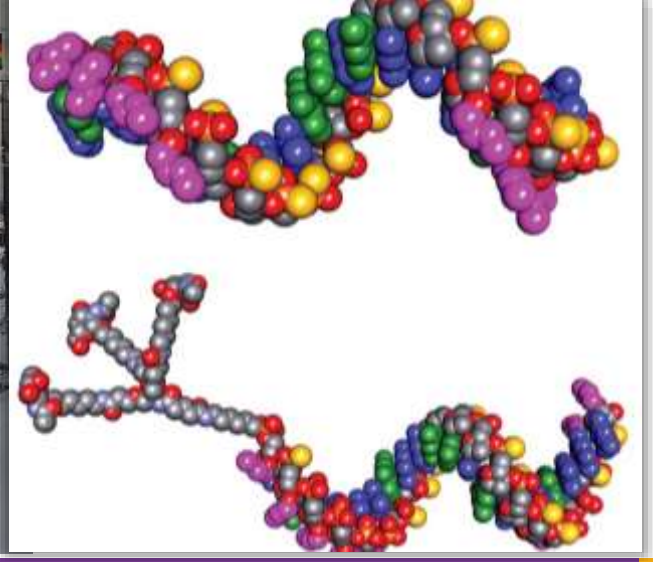


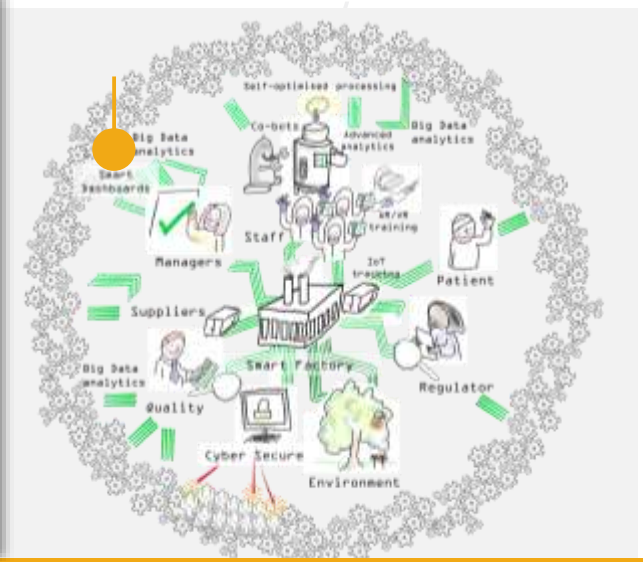
Figure 1 – A product set with 'traffic light' label and percentage relative to a benchmark

Source: Reproduced from Figure 2.7 in Elsen et al. (2019)

The one tool we have that reduces cost, improves sustainability whilst not compromising supply is……

Innovation





GC1 – Continuous Direct Compression Digital Test-Bed

We believe stream-lined, agile formulation technologies and digital twins should be employed in drug product development and commercial manufacture, thereby reducing the development burden, cost to patients and carbon footprint of medicines production

GC2 – Automated Clinical Trial Packing & QP Release Platform

We believe patients deserve faster and cheaper supply of clinical trial medicines, with much less waste

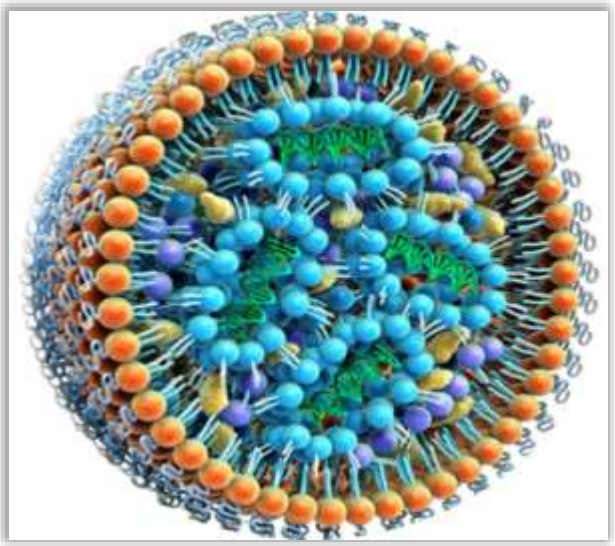
GC3 – Cost Effective & Sustainable Oligos Manufacturing

We believe a paradigm shift is needed in the manufacturing of oligonucleotides to ensure this exciting class of new medicines will be available to treat patients at affordable prices and in a sustainable way

Digital Manufacturing Innovation Programme

We believe Digital innovation sits at the core of our operation and will inform our operational strategy and deployment as we create and de-risk novel technologies for our partners

Industry 4.0 is critical to delivering a step change in productivity, carbon efficiency and compliance



Lipid Nanoparticles

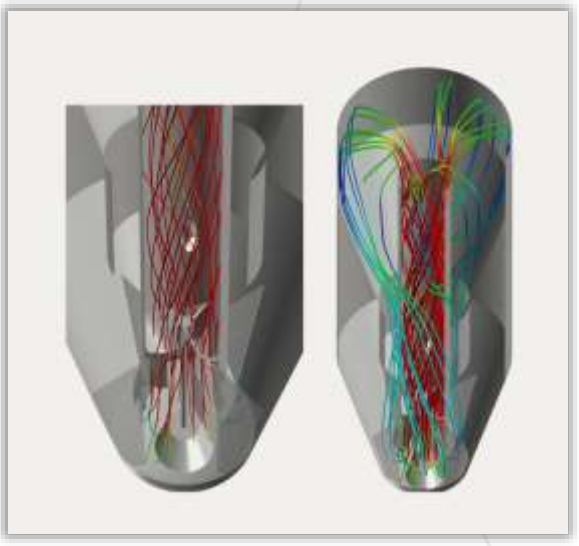
- Significantly enhance *in vitro* assays so they're more predictive of biological efficacy & safety
- De-risk late phase clinical trials and accelerate the pipeline of new RNA-LNP vaccines and therapeutics for patients
- Finalising the scope

Smart Bioprocess Development

- Develop & deliver an automated platform to build product agnostic predictive models for cell culture and purification
- Integrate complex characterisation, AI data analysis, and next generation sequencing
- Designing a proof of concept study

Oligonucleotide Man Innovation Centre

- £20m "Chemistry Facility" to develop innovative approaches to synthesis, purification and Analysis
- £50k funds for feasibility study (Q4 '22)
- £500k funds for Detail design study (Feb23)



Continuous Crystallisation

- Building on the CMAC research programmes and recommendations from their Industry Board

Real Time , Carbon Dashboard

Generation

Building Energy Usage

Facility Equipment state

Production Machinery State

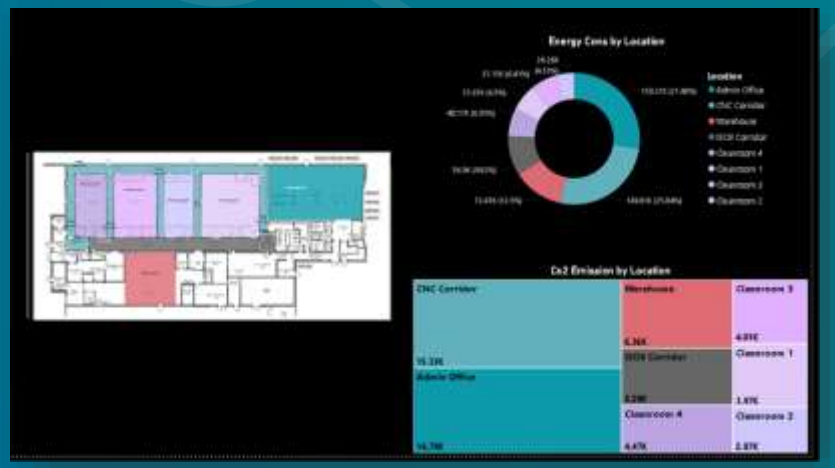
Data Infrastructure

Data Ingestion
Extract data from source application into Data infrastructure

Data Lake
Central repository or data in the cloud.

Data Transformation
Add meta-data and context to data to enable it to be combined

Data Warehouse
Structured store of data to present to BI and analytics



Carbon Dashboard

NCL-CPI ‘Living-Lab’

- **Public – Private – Partnership**
  A unique consortium mode under the umbrella of the **UK-India NetZero Innovation Centre (NZIC).**

- **A joint initiative of CSIR-NCL, India and CPI (part of the UK’s Catapult Network)**
  driving decarbonisation of India’s pharma and fine & specialty chemical industry through innovation and thought leadership.

- **Phase-1 objectives :**
  - Build a platform for **sharing essential knowledge** about continuous and solvent-free manufacturing technologies
  - Benefit the overall **ecosystem** of pharma and fine & specialty chemicals sector
  - Industrialise **digitally enabled** manufacturing based on NCL and CPI’s extensive experience.
  - Foster innovation, translation and market demonstration through a **triple helix** partnership of R&D labs – Industry – Government.
  - Showcasing flow chemistry and continuous manufacturing to **regulators** to enable faster adoption.
  - Mostly pre-competitive research and capacity building.

Living Lab Phase 1 - Headlines to date

- In operation since Oct 2024
- 20 Cr budget funded; about one third each from Government grants (UK and India), NCL and industry partners.
- Formally opened Inargurated 20 Feb 2025 by Padma Shri Dr Sivaram
- Includes
  - Lab-scale flow synthesis facilities for platform
  - A modular & multipurpose skid for continuous manufacturing and downstream processing for L-L, G-L, G-L-S reactions as well as mechanochemistry.
  - Digital twin of the skid enabling improved process control and safety, QC, data traceability
  - Commercial modeling (Business case for change)
- Demonstration that flow synthesis does not necessarily need high capex investments!
- Development of a “choice metric” to determine, in silico, if a given reaction can be beneficially carried out in flow.
- Training/ upskilling/ reskilling staff from Pharma and other industries.
- Newsletters and white papers to document global trends and support policy decisions.

NCL-CPI Continuous Flow Synthesis Rig

Various flow synthesis and continuous mechanochemical synthesis skids planned under the Centre

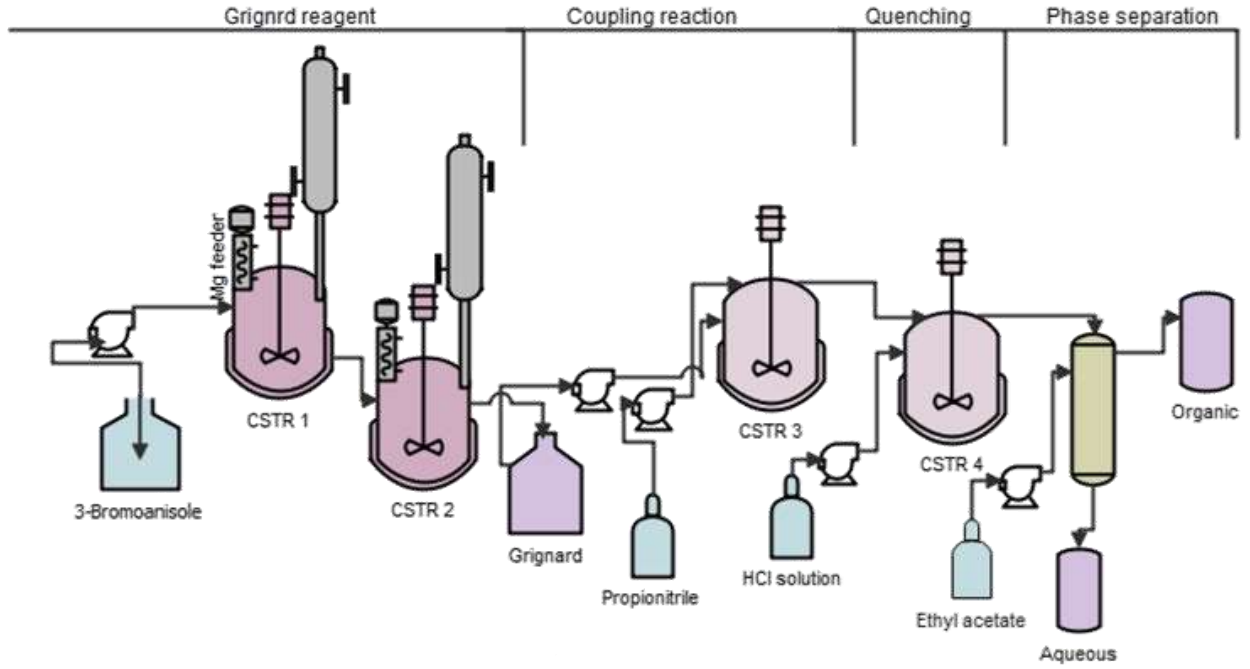
Grignard reactions	Chlorination, Bromination & Fluorination	Aromatic nitration	CS_2 based chemistry	Lithiation
Esterification	Oxidations including ozonolysis	Diazotization and related chemistry	Sulfonation	Ultrafast reactions
Polymerization (radical, emulsion, anionic, etc.)	Photochemical reactions	Pyrolysis and cracking	Gas/Vapour phase reactions	Hydrogenation
Amidation	Solvent Free reactions	Fusion reactions	Cynation and associated chemistry	Electrochem. in flow

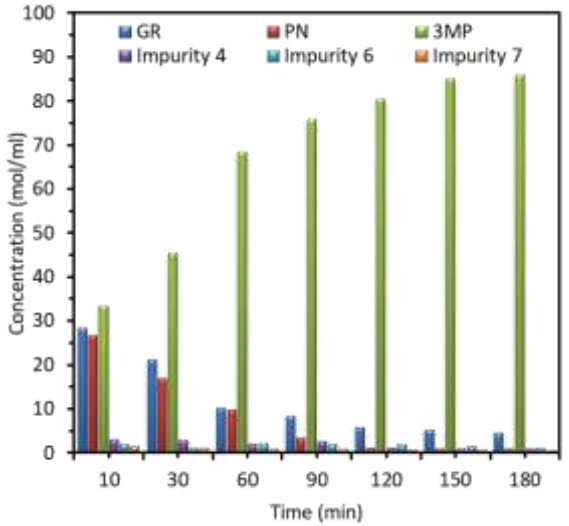
Continuous flow Grignard reaction for API synthesis

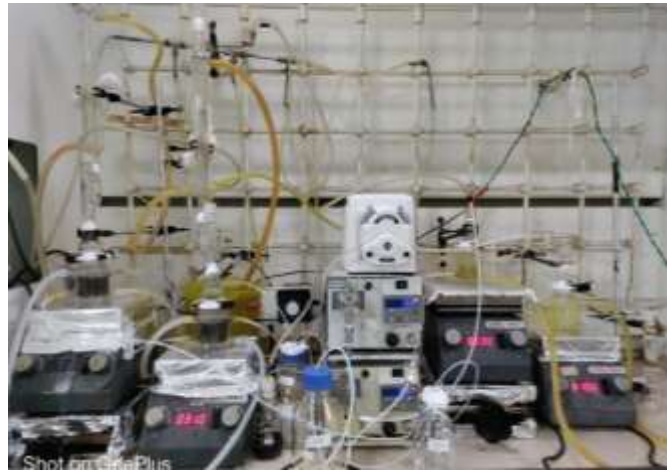
- Model case study: 3-methoxypropppphenone is an intermediates for synthesis Tramadol (oral pain-relieving medicine)

Mode →	Batch	Continuous
Reaction time (Hours)	8-10	4
% Conversion	>95%	>99.7%
% Impurities	5 – 8 %	< 1%
% Byproducts (dimer)	4 – 6%	< 2%
The final yield	48%	84–86%
Footprint for 1 TPD (m^2)	X	0.3X
ROI (Years)	X	0.2X

- **Moving to pilot plant:**
  - Fully automated plant
  - Developing guidelines for scale-up
  - Continuous recovery and reuse of the solvents
  - Timeline: June 2025







Structure of the ‘Living Lab’

Living Lab, part of the Centre for Sustainable Continuous Manufacturing, NCL

Founding partners		Industry partners		
CSIR-NCL, India	CPI, UK	Tier 1: Core members	Tier 2: Technology Partners	Tier 3: Consortium members:
Competencies in flow synthesis, reactor design and scale-up. Experience of working on large number of projects in these areas.	Strong footprint in translational research and innovation including medicines manufacturing, digitalisation, formulations and business engagement models	Up to 8 Large Fine & Specialty Chemicals & Pharma companies	Up to 6, Niche technology owners Partners in the Living Lab	Up to 20 Mid-size chemical and pharma companies
		On SAC & TAC	On TAC	Access to the lab-scale skids

Strategic Advisory Committee (SAC):

- To advise on the strategic direction of the Centre.
- Frequency – Once a Quarter

Technical Advisory Council (TAC):

- To monitor the specific project activities in the Centre as identified by the SAC.
- Frequency – Once every two months

Tier-1, Tier- 2 & Tier-3 members for Phase 1

Tier 1 members

- Sun Pharmaceutical Industries Ltd
- Aarti Industries Ltd
- USV Pvt. Ltd
- Glenmark Life Sciences Ltd. (Alivus)
- Anthem Biosciences Ltd

Strategic partners:

- Indian Pharmaceutical Alliance (IPA)

Tier 2 members

- GMM Pfaudler Ltd
- Corning India Ltd

Tier 3 (Announced on Jan 30, 2025): Agreements in progress

- Alps Chemicals Pvt. Ltd.
- Flokem Ind. Pvt. Ltd.
- Gharda Chemicals Ltd.
- OC Specialty Chemicals Pvt. Ltd.
- Jay Chemicals Pvt. Ltd.
- US Pharmacopia Ltd.

Initial thoughts and ambition on proposed Phase 2

The Phase 2 plans are being jointly evolved by the Founding members, with the Strategic Advisory Committee and other key stakeholders in India and the UK

Currently exploring:

- Scale of the activity (GMP vs non-GMP, pilot or demonstration scale etc)
- Scope (small molecule pharma versus other modalities and other applications)
- Engagement models with industry (**PPP vs private** and **non-profit vs for-profit**)
- Structure, Governance and operational models
- Location

Thank you

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Extra slides

Why continuous manufacturing?

- No batch-to-batch variations.
- Significant decarbonisation due to
  - Higher conversion and better selectivity of products, thus lower emissions from downstream purification.
  - Lower utility costs.
- Improved process control and safety.
- Significant reduction in manufacturing time.
- Smaller footprint.
- Staying with competition in global markets.

Why has continuous manufacturing not been adopted widely?

- Perception that flow reactors are “expensive”.
- Lack of a “choice metric” to decide flow vs batch for a given process chemistry.
- Non-availability/ lack of access to continuous downstream separation/purification techniques.
- Non-availability of trained/skilled HR in flow chemistry.
- Lack of ecosystem to help derisk flow synthesis technology from lab to pilot to commercial scale.

The Centre for Sustainable Continuous Manufacturing will primarily address these barriers in Phase 1