I-SEE Seminar; Sustainable Manufacturing

UNIVERSITY OF BATH

Continuous Crystallisation – a Route to Sustainable Manufacturing in the Pharmaceuticals and Fine Chemicals Industries

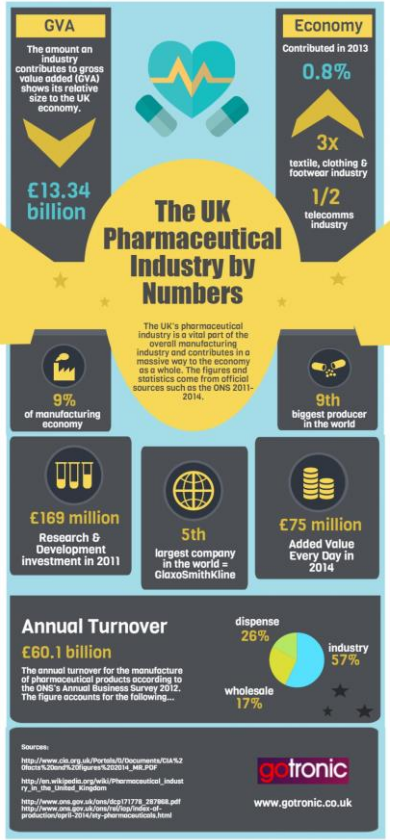
Chick Wilson, University of Bath

Context

UNIVERSITY OF BATH

The Importance of the Industry

- £60Bn chemical and pharmaceutical industry; UK's largest manufacturing exporter (CIA/ONS)
- The chemical and chemistry-using industries' growth strategy (IChemE): increase GVA by 50% from £195Bn to £300Bn
- Pharmaceutical manufacturing: exports of £24Bn, trade surplus of £4.9Bn (2012)



UK Pharmaceutical and Fine Chemicals Industry

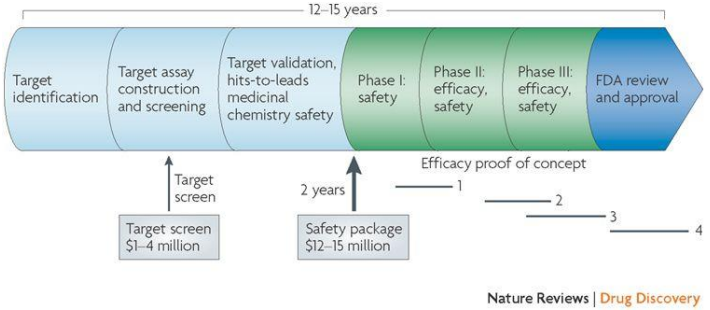
Constraints

Infrastructure, Drug Development Timescales

BASF Ludwigshaven

- Manufacturing Plants
  - Large, substantial capital commitment
- Drug Development Pipeline
  - Development time 12-15 years to market; up to $1bn cost
  - *ca.* 1 in 10,000 drugs successfully translated to therapy

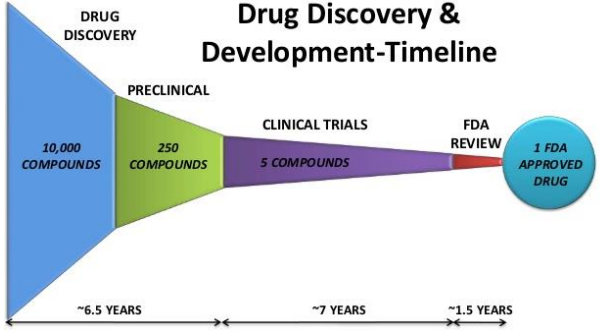
→ Risk Aversion

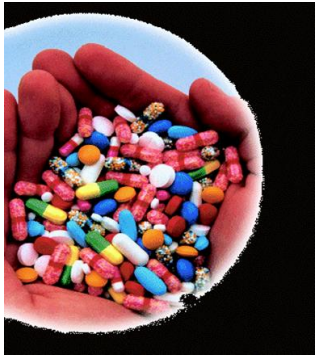


The Focus on Optimised Manufacturing

Drug Development Pipelines drying up wrt new compounds

- Disinvestment in core R&D for drug discovery and development
  - Focus on buying in new discovery products
- New materials at a premium
  - Particularly few blockbusters coming through
- Focus on extracting maximum value from existing portfolio
  - Better formulation (bioavailability); more effective manufacturing; smaller dosage





Continuous Crystallisation:

Towards sustainable manufacturing of pharmaceuticals

- Continuous crystallisation: Universal application - >80% pharmaceutical products, >60% fine chemical products are made in crystalline form
- Focus on manufacturing optimisation for profit gives a real opportunity for developing sustainable, energy-efficient and environmentally-friendly approaches…

- … Why, and How??

Continuous Manufacturing:

Evolution of Manufacturing Technology for Chemicals

c.1556

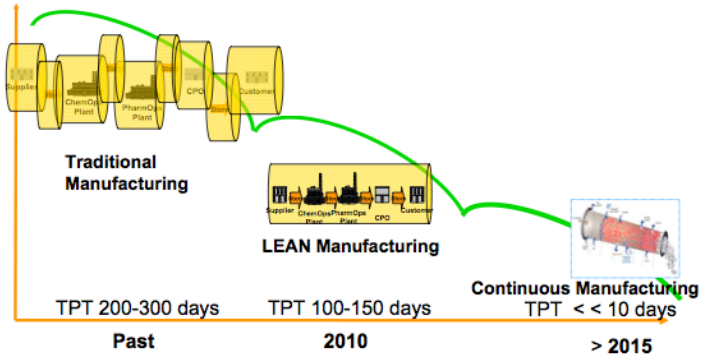
1956

2008

Not the White Heat of Technological Revolution

Continuous Manufacturing:

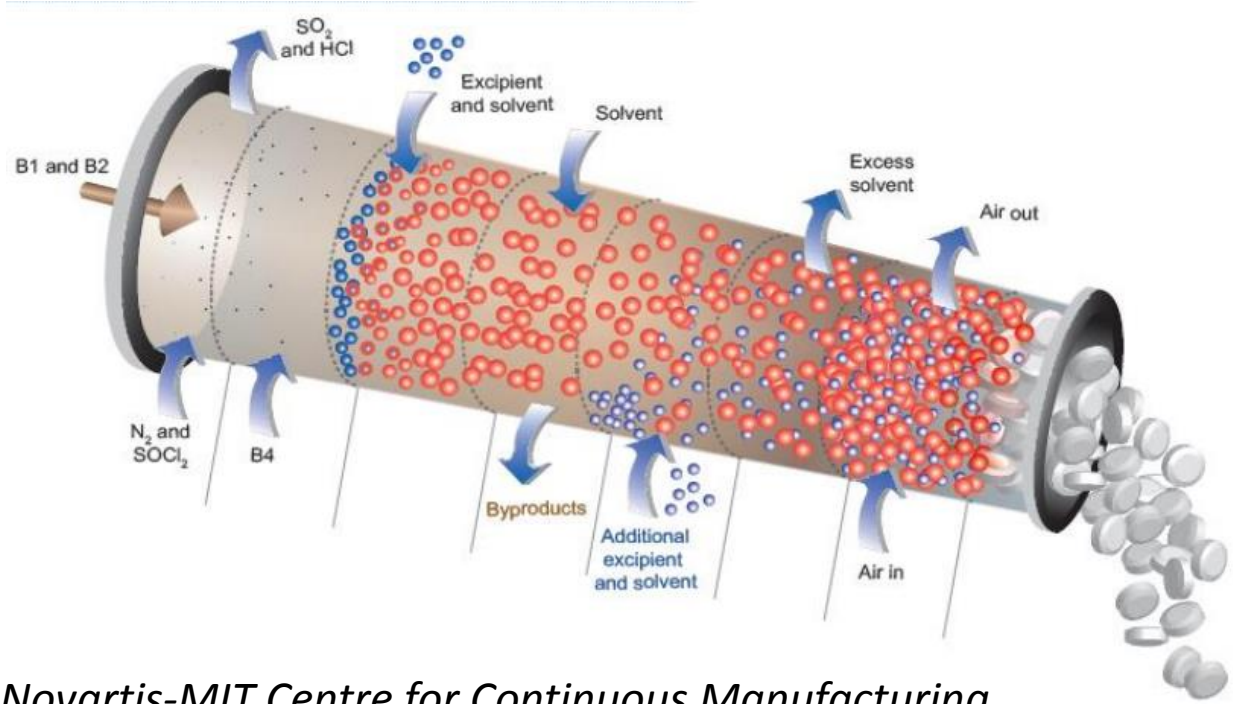
Sustainability, Energy and Environmental Benefits



- Sustainability; footprint reduction (40-90%, 25-60% capital)
- Lower running costs (25-60%); reduced & recoverable solvent, less energy
- Speed of scale-up of platform technologies
- Controllable quality
- Small batch, personalised medicine

Sustainable Manufacturing:

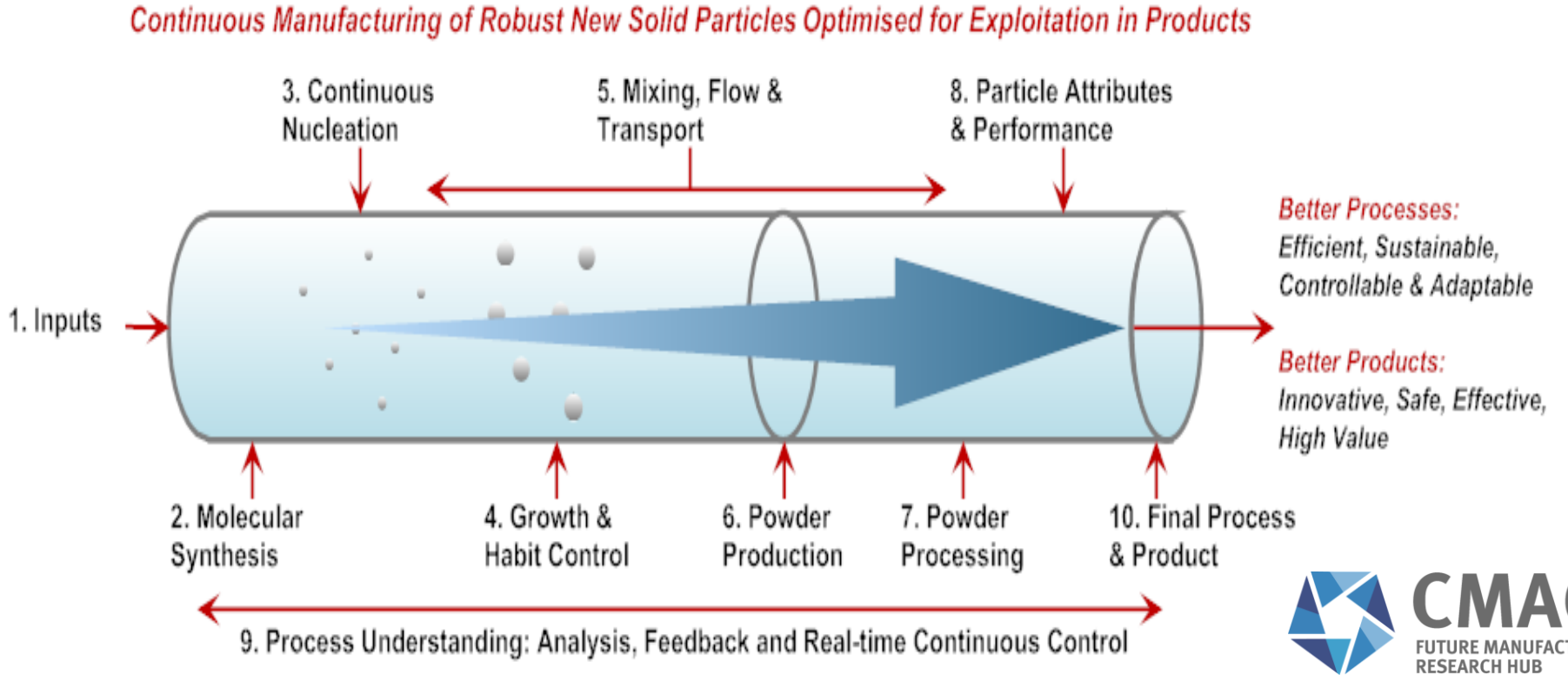
Integrated Pipeline for pharmaceutical manufacturing



Novartis-MIT Centre for Continuous Manufacturing

Sustainable Manufacturing:

Integrated Pipeline for pharmaceutical manufacturing



UNIVERSITY OF BATH

CMAC FUTURE MANUFACTURING RESEARCH HUB

Technical Challenges

Platforms

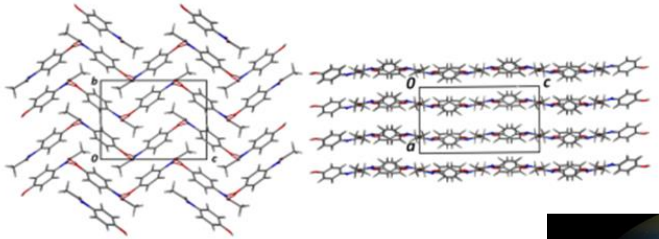
- Development of platform continuous technologies
- Pre-competitive collaboration essential, and achievable
- Best science, Engineering, Design, Manufacturing, Supply Chain capabilities
- Unified approach *wrt* regulators

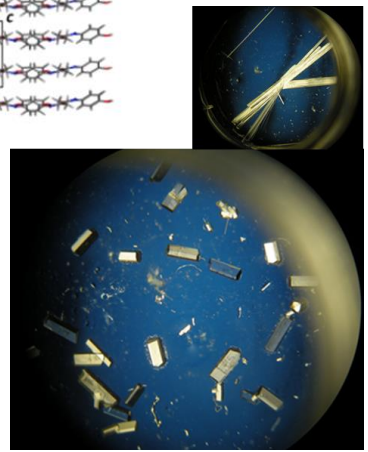
Products

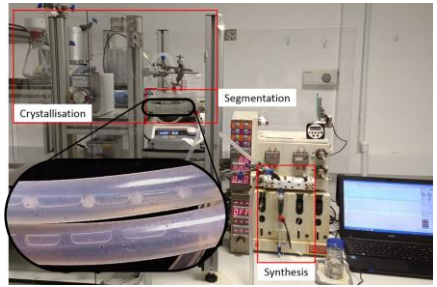
- Ensuring equivalent of batch-to-batch reproducibility
- Delivering QbD imperatives

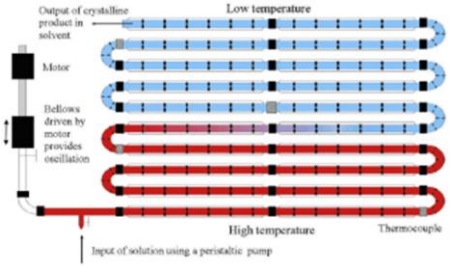
Continuous Crystallisation for Manufacturing Research at Bath: From Platforms… to Products

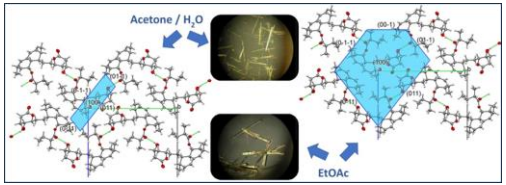
UNIVERSITY OF BATH

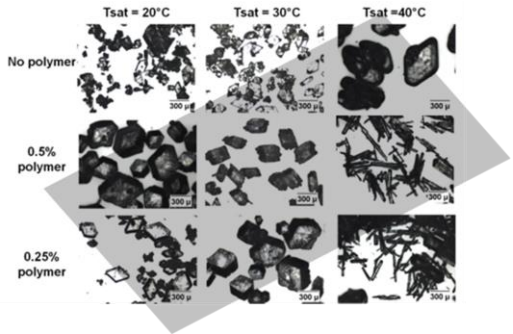


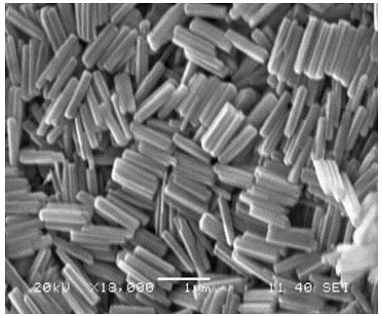


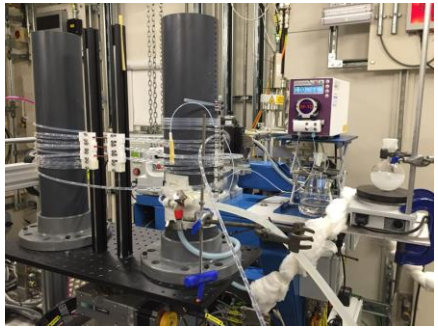












CMAC and its Approach

UNIVERSITY OF BATH

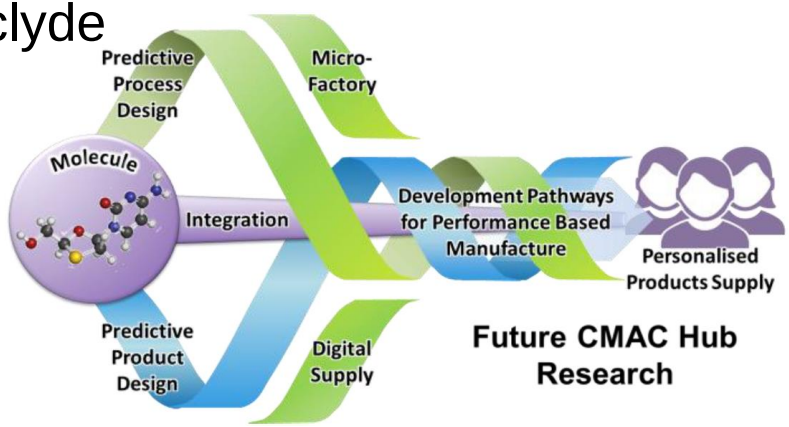
EPSRC Future Manufacturing Hub

Multi-Disciplinary, Multi-institution

- £50M Hub, 2016-2023;
  Director: Alastair Florence
- Partners: Bath, Cambridge, Imperial, Leeds, Loughborough, Sheffield, Strathclyde

Academic-Industrial partnership

- Eight Tier-1: AstraZeneca, Bayer, GSK, Lilly, Novartis, Pfizer, Roche, Takeda
- Wide range of Tier-2 industrial members (users, suppliers, business)

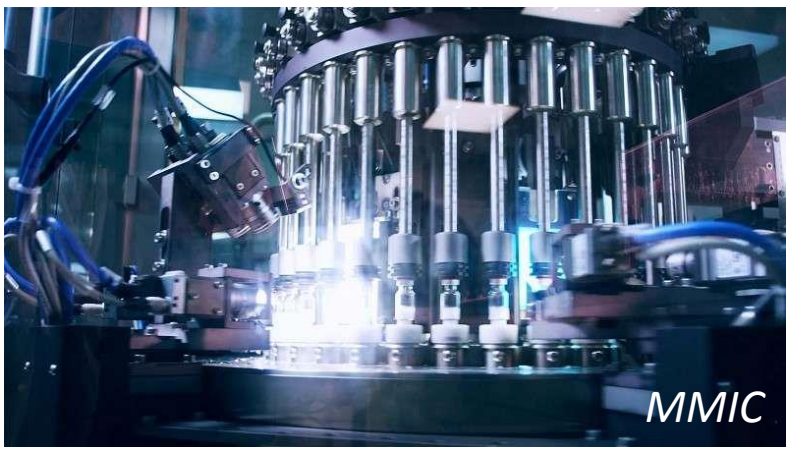


EPSRC · Strathclyde Glasgow · Bath · Cambridge · Sheffield · Imperial College London · Leeds · Loughborough · GSK · AstraZeneca · Novartis · Bayer · Lilly · Takeda · Roche

Non-Technical Challenges

Economics, Policy, Regulatory barriers to adoption

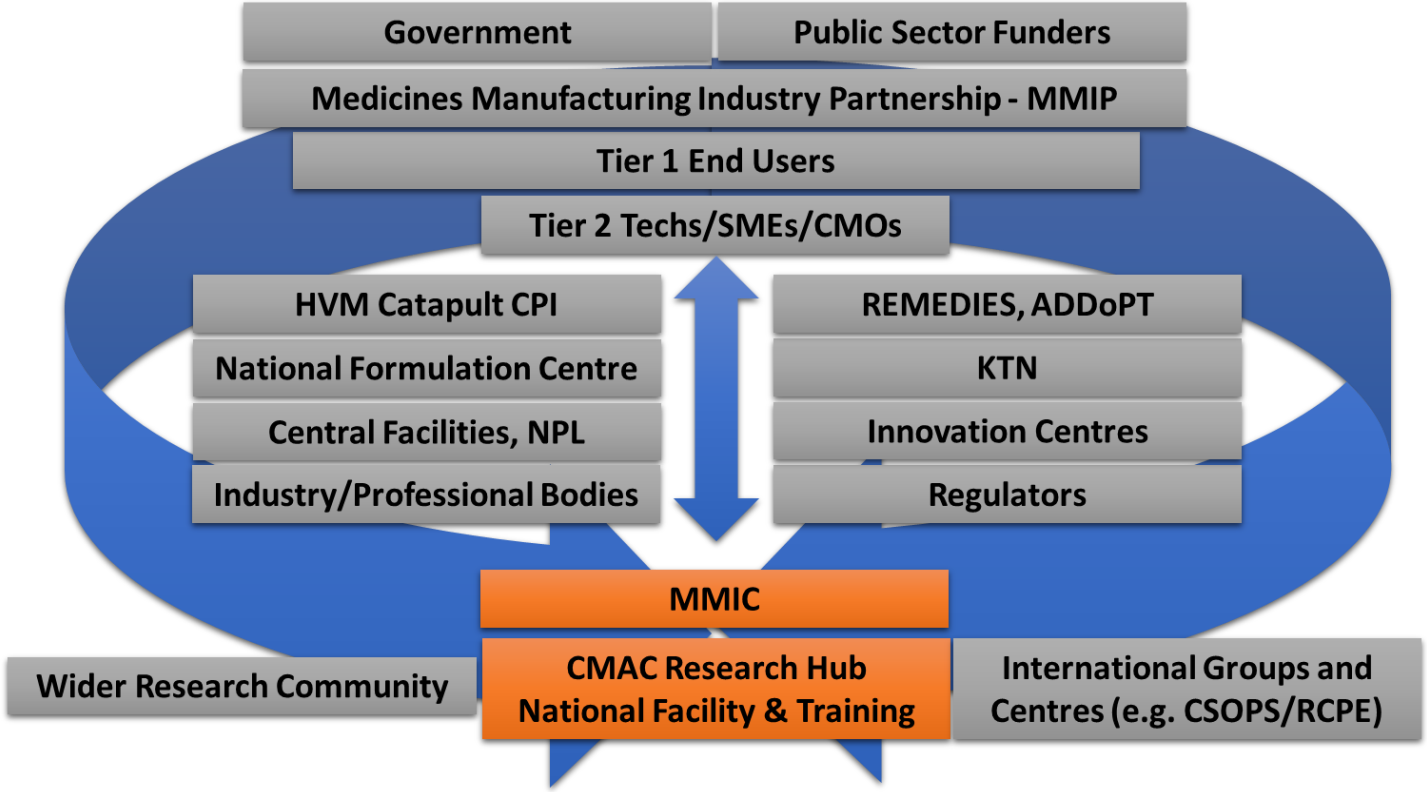
- Traditional risk averse attitude; existing technologies well established, reliable, trusted – opposition at technical level
- Advance sustainability arguments
- Persuade CFO to replace $Bn plant with continuous
- Create political and economic environment that is supportive for long-term manufacturing investment



- Partner with regulators (MHRA, EMA) to license new manufacturing paradigm (FDA had licensed just two CM processes by 2016, even with enlightened and engaged leadership)

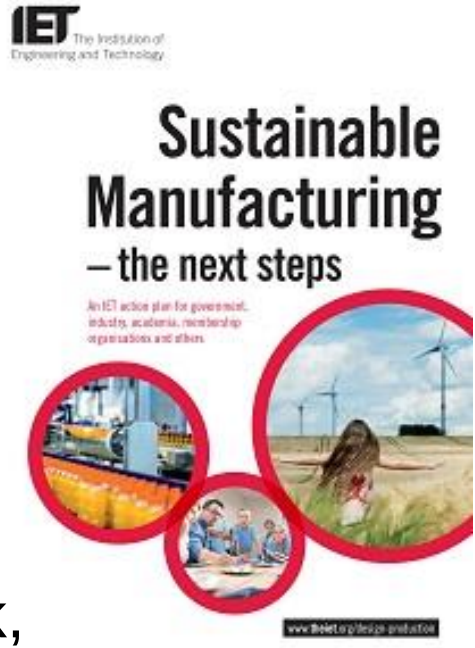
The Landscape

Investment, Research, Policy & Regulation



The Future: Next Steps

- Scientists and Engineers: Deliver Compelling Solutions
- Industry: Continue Pre-Competitive Co-operation; Take the Risk to Invent in Continuous Plant
- Regulators: Agility and responsiveness
- Politicians: Consistent Regulatory framework, Environment for UK Manufacturing Industry



IET 2017