



Innovative Medicines Initiative

Sustainable Chemistry – Delivering Medicines for the 21st century

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Need for public-private collaboration



- Discovery of sustainable synthesis methodologies is a long-term (> 3 years) endeavour
 - Critical expertise lies predominantly in academia
 - Implementation is done in the pharmaceutical industry to serve innovative medicines
- Opportunity to develop an integrated long-lasting leading position in Europe on sustainable chemistry through this public-private collaboration
- Sustainability is a worldwide concern
 - European pharmaceutical industry needs to support this initiative for being able to deliver new innovative medicines to the patients in the future



Objectives of the full project

- Discovery of new synthetic methodologies for the development and manufacture of small molecules for innovative medicines
 - More sustainable / efficient than the current state
 - Novel organic / organometallic catalysis
 - Process intensification / flow chemistry
 - Bio catalysis
 - Synthetic biology
 - Exemplification of sustainable chemistry principles into graduate medicinal and process chemists education and training with hopefully broader impact on the whole European academic community.
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Pre-competitive nature

- The primary intellectual property associated with a drug is the molecular structure rather than the synthetic steps to assemble the molecule
 - Currently, pharmaceutical relies on public sector researchers to provide new reaction methodologies for industrial use
 - all companies use similar types of reactions
 - Similar collaborations have demonstrated the ability for multiple companies to work in this space pre-competitively (e.g., ACS Green Chemistry Institute Pharmaceutical Roundtable ®)
 - Having a workforce educated in sustainable chemistry is a broad skill needed across the industry
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Expected impact on the R&D process



- Use of improved and new sustainable transformations and methodologies will trigger
 - access to new targets not achievable by current state of the art in chemistry and biotechnology
 - easier access to quantities of API for clinical studies
 - faster development of eco-efficient processes for new drugs with better mass efficiency than currently
 - broader applications of enzymatic and biological processes

Suggested architecture of the project



- EFPIA consortium is proposing work packages of interest for improving the sustainability of the chemistry to deliver innovative medicines.
 1. Definition of areas of focus
 - agree on scope of other work packages
 2. Work packages to address recognised sustainability gaps.
 3. Educational program
- Applicant consortium is expected to address all the research objectives and make key contributions in synergy with the EFPIA consortium.

Work package 1: Survey of chemical landscape



Aim:

- to understand transformations / synthetic methodologies of concern beyond 2020.
 - Update 2007 paper published by the Green Chemistry Institute Pharmaceutical Roundtable.
 - Consider scarcity of metals as catalysts
 - Transformations with poor green metrics
 - Transformation which can benefit by use of more benign solvents.
 - Synthetic biology tools, methodologies and targets
 - Flow chemistry

Aims:

- to develop more sustainable catalytic methods for complex molecules
 - use organometallic / organic catalysts (potentially in combination).
 - minimise amount of catalyst utilised (recovery, leakage, etc...).
- to use continuous / flow chemistry to safely enable chemistry that are not practical for a batch process & enable process intensification.
 - use of micro reactors

Work package 3: Biocatalysis



Aim:

- Sustainable and cost effective synthetic routes via biocatalysis
 - need for a greater range of enzyme types capable of accepting a broad range of substrates.
 - design and development of new enzymes by genetic engineering
 - preferred reaction types to address:
 - Ester to amide in one step.
 - Redox reactions avoiding Os, Cr, Pt, Pd etc...
 - Fluorination using inorganic fluoride sources.
 - Hydroxylation (likely whole cell approach)



Aim:

- To conduct cascade reactions in a cell.
 - Multiple different reactions being performed with non-native enzymes in a single fermentation.
- To achieve this over-arching aim will require:
 - A small number of biological host organisms
 - Genetically stable recombinant systems
 - Non-pathogenic, predictable, suitable for scale-up of cell cultivation and downstream processing.
 - Demonstration of the technology (artificial biosynthetic pathways).
 - Greater understanding of the limiting factors

Work package 5: Chemist Education



Aim:

- Adoption of sustainable methodologies by chemists.
 - Seek to demonstrate that early adoption of green chemistry methodologies has the potential to remove some of the reliance on increasingly scarce reagents.
 - Adopt sustainable routes teaching in postgraduate programs.
 - Development of sustainability metric tool suitable for use in early development by academia and industry.
 - Industry can provide materials and syntheses, but need the consortium to deliver greener syntheses and evolve a broader educational approach.
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Expected contributions of the applicants



- Deliver scientific proposals based around work-packages using applicants experience in fields of catalysis, flow chemistry, biocatalysis and synthetic biology.
 - Different work packages require different skillsets.
- A strong experimental component is essential.
- Access to suitably equipped laboratories in which the work can be conducted.
 - Internationally recognised labs working with one another.
- Ability to work openly with members of the consortium to progress proposals, tuning each work package.
- Deliver solutions to the problems outlined in the work packages.
 - Solutions to real-world issues, not just an exercise.
- Strategies to address improving education in sustainability should be included by the applicant.

Expected (in kind) contributions of EFPIA members



- **Make scientists working in pharmaceutical industry available to **exchange and collaborate** with academics and universities on agreed subjects from work packages**
 - company affiliates, PhD's or post-Doc's
 - part of their objectives
 - have seniority and experience in the field
 - working in parallel on a similar topic/field
 - **Provide the necessary support and guidance**
 - to establish the working program
 - to track progress
 - to share the decision on subject evolution
 - to bring the technical input when needed
 - to propose sustainable chemistry educational material
 - **Industry to include experimental work in house towards the deliverables, and providing support with things like assays, substrates, scale-up to consortium partners**
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What's in it for you?

- Opportunity to work on practical “unmet chemical needs” and to discover new methodologies for better ways to synthesise innovative medicines for patients
- Opportunity to gain deep insight into industry synthetic challenges
- Opportunity to network with other scientists from European pharmaceutical industry, SMEs and academia
- Work on the sustainability of our European pharmaceutical industry coping with future environmental regulations
- Educate future generation of R&D scientists in pharmaceutical industry on sustainable chemistry



Key deliverables of full project

- Discovery of new synthetic methodologies, for the synthesis of small molecules, which are more sustainable and efficient than the current ones
 - Exemplification expected to be delivered through each of the proposed work packages with common “sustainability” metrics
- Recommendations for graduate training and education programs to ensure future generation of medicinal and process chemists fully understand and apply sustainable chemistry principles



Take away message

- Sustainable chemistry for the development of new medicines is the only way to keep on competitiveness of our pharmaceutical industry
 - By innovation to give access to new targets not achievable by current state of the art chemistry
 - By innovation to maintain cost efficiency of our processes
 - By innovation to cope with on coming regulations on sustainable chemistry towards our future environment
- Public-Private collaboration is key to improving the competitiveness of the European pharmaceutical sector

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