

Title of proposed program: New Technologies to Accelerate Therapeutic Synthesis

What is the major obstacle/challenge/opportunity that the Common Fund should address?

As fundamental understanding of disease biology advances and the number of therapeutic targets increases, rapid access to clinical quality drug substance and drug product to enable and accelerate translation becomes an ever growing need. At the same time, synthesis of drug substance (API) and manufacture of drug product (formulation) of clinical quality on industrial scale and in a controlled and reproducible way is still a highly resource- and time-consuming undertaking. Both pharmaceutical and generic industries are facing increasing pricing pressures, coupled with rising manufacturing cost. There is a need for technologies and methodologies that will accelerate synthesis and formulation of drugs. These technologies would be largely in the pre-competitive space.

While relevant to drugs for all diseases, the impact will be especially high in the case of neglected tropical diseases (NTDs) that affect an estimated one billion people, primarily in the developing world. Even for NTDs in which treatments are available, one of the major problems is insufficient access to existing medications, due in part to the high cost of existing drugs and related limited supply. Drugs used for NTDs are typically off-patent. In many cases, synthetic processes for manufacturing these drugs and formulations were developed in the 1970s or earlier. New synthetic methodologies and new technologies have been developed since then (e.g., advances in catalytic asymmetric synthesis, transition metal-catalyzed transformations, enzymatic biotransformations, use of flow chemistry techniques, advances in formulation development and drug delivery systems, etc.).

In the case of NTDs, there is an added opportunity to apply existing modern technologies to develop low-cost manufacturing processes and more palatable formulations for existing off-patent drugs that would rely on inexpensive and easily available raw materials, avoid use of overly expensive, highly-specialized equipment, and make these processes available to low-cost “low-tech” manufacturers in the developing world. This would lower the cost of drugs, increase supply, and improve patient access in the developing world.

What would the goals of the program be?

1. Develop methodologies and technologies in the pre-competitive space to accelerate synthesis and formulation aspects of the drug development process;
2. Develop low-cost synthetic processes for drugs (e.g., for NTDs) that would rely on inexpensive and easily available raw materials and avoid use of overly expensive, highly-specialized equipment;
3. Develop improved formulations addressing issues with approved treatments that would result in improved compliance: longer acting products, improved palatability, availability of pediatric-specific formulations, etc.;
4. Provide open access to a single resource with detailed synthetic processes and formulations for existing off-patent drugs for NTDs to all interested parties (e.g., NGOs, low-cost “low-tech” manufacturers in the developing world).

Why is a trans-NIH strategy needed to achieve these goals?

The program involves diseases of interest to multiple ICs. A coordinated effort is needed to ensure input from, and ability to capitalize on, the diverse expertise of investigators from different ICs. There is already interest on the subject in several academic groups (e.g., Dr. Joseph Fortunak of Howard University, Dr. B. Frank Gupton of Virginia Commonwealth University), as well as the IQ Consortium of pharmaceutical companies. Collaboration with the NSF Catalysis and Biocatalysis Program should be considered, and interest from DOD and WHO is expected, as well.

What initiatives might form the strategic plan for this topic?

Initiatives for the program may include:

1. Development of new practical synthetic methodologies to accelerate drug manufacture;
2. Development and advancement of new technologies in the pre-competitive space that would lower manufacturing cost for APIs and formulations;
3. Optimization of engineering design of new technologies (e.g., flow reactors) that would allow their easy and low-cost implementation;
4. Process R&D to develop low-cost synthetic processes for manufacture of off-patent drugs for NTDs using novel methodologies (e.g., catalytic asymmetric synthesis, transition metal-catalyzed transformations, enzymatic biotransformations, use of flow chemistry techniques, application of principles of green chemistry, etc.);
5. Process R&D to develop newer, more convenient formulations for drugs for NTDs;
6. Open access database of synthetic processes for manufacture of Drug Substances for NTDs;
7. Open access database of formulations of Drug Products, including quantitative compositions of new formulations for existing treatments of NTDs.

If a Common Fund program on this topic achieved its objectives, what would be the impact?

Development of new practical synthetic methodologies and low-cost manufacturing technologies will lower the cost of drug development and medical care in the long term. In the short term, lowering the cost of existing drugs for NTDs should result in improved patient access to medications, leading to a more immediate effect of increased survival rates and improvement in quality of life for the estimated one billion global population affected by NTDs.