



2024 ACS Green Chemistry Institute Pharmaceutical Roundtable Research Grant for New Methods or Strategies for Greener Peptide Synthesis and/or Purification

The [ACS Green Chemistry Institute Pharmaceutical Roundtable](https://gci.acs.org) (GCIPR) is a partnership between the ACS Green Chemistry Institute® and companies in the pharmaceutical and allied industries committed to integrating the principles of green chemistry and engineering into synthesis and production. Current members are AbbVie, Amgen, AstraZeneca, Bayer, Biogen, Biohaven, Boehringer-Ingelheim, Bristol-Myers Squibb, Lilly, F. Hoffmann-La Roche Ltd., Gilead, GlaxoSmithKline, Ipsen, Johnson & Johnson, Merck & Co., Merck KGaA, Darmstadt, Germany, Neurocrine, Novartis, Novo Nordisk, Pfizer, Sanofi, Takeda, UCB Pharma, Vertex, and the ACS Green Chemistry Institute. Associate members are Ampac Fine Chemicals, Asymchem, Aexplora, Bachem, CatSci, Codexis, Hikal, Hovione, InnoSyn, PharmaBlock, Pharmaron, Polypeptide, PHT International Inc., Porton, Sai Life Sciences, Solara Active Pharma Sciences Ltd., STPharm, and WuXi AppTec. Affiliate members are Corteva Agriscience, FMC and Zoetis.

The ACS GCI Pharmaceutical Roundtable is seeking a one-year R&D commitment to assist the Roundtable's green chemistry initiative to develop strategies for greener synthesis and purification of peptides. Proposals are invited from public and private institutions of higher education worldwide. This collaborative project is intended for a student within the selected Principal Investigator's research group. One grant is planned to be awarded and the total award is limited to \$80,000 for a grant period of 12 months. Interested PIs are required to provide a written proposal describing the investigator's capability to carry out the Roundtable's proposed research. Deadline for receipt of proposals is **May 17, 2024, at 5 p.m. EST**. All submissions must be made in our application portal: <https://gci.acs.org>. The Principal Investigator with the selected proposal will be notified by **September 1, 2024**. It is expected that research will commence in the principal investigator's lab no later than **October 2024** and last 12 months.

Requirements for Submission

Proposals will only be accepted from public and private institutions of higher education. The grant is not limited to institutions in the United States. Proposals must be submitted in our application portal <https://gci.acs.org> through the appropriate institutional office for external funding. For international submissions, if there is no comparable office, submit a PDF of a letter signed by an appropriate university official recognizing the terms of the grant.

Detailed Project Description

Peptides and peptide conjugates are of increasing interest as new drug candidates within the pharmaceutical industry. [Unfortunately, the synthesis and manufacture of these compounds tend not to be particularly green for several reasons.](#) Firstly, platform technologies such as solid-phase synthesis are often used to prepare peptides which generate large quantities of solvent-based waste. In addition, product purification is typically achieved by chromatography, while buffer exchange or product concentration may be accomplished using tangential flow filtration (TFF). These operations can also be solvent intensive, and in the case of solid-phase synthesis may also employ reagents and solvents that

are not green such as DMF, NMP and dichloromethane. An excess of reagents is also often employed to obtain complete conversion, where many of these reagents have safety concerns as well. Finally, dilute conditions may be favored in the synthesis of these compounds, for instance in the case of peptide macrocyclization or to limit aggregation in the preparation of peptides or peptide conjugates.

The goal of this work is to develop strategies for greener synthesis and purification of peptides. These may include, but are not limited to:

- Novel coupling reagents, resins, protecting groups, and/or solvents that are green, efficient, safe and/or cost-effective.
- Alternative synthesis techniques, such as green and cost-effective amide bond formation methodologies:
 - Native Chemical Ligation
 - Chemo-Enzymatic Peptide Synthesis
 - Tag Assisted Liquid-Phase Peptide Synthesis or related approaches
 - Electrochemistry
 - Mechanochemistry
- Hybrid strategies that leverage recombinant expression for peptide synthesis (i.e., semi-synthesis) such as:
 - Expressed Protein Ligation or related approaches
 - Incorporation of unnatural amino acids in recombinant systems
 - Formation of amidated peptides using recombinant technologies
 - Conjugation / mixed modality strategies
- Use of flow chemistry techniques for peptide preparation, peptide conjugate preparation, and/or isolation.
- Greener peptide conjugation or modification methods.
- Solution phase fragment condensation - preferably utilizing green solvents (for further solvent guidance, refer to the [ACS GCI Pharmaceutical Roundtable Solvent Tool](#) or [CHEM21 Solvent Selection Guide](#)).
- Reduced chromatography or chromatography-free systems.
- Implementation of alternative purification approaches, such as membrane-based approaches or other forms of chromatography, and/or isolation methods.
- Other innovations which reduce [PMI \(Process Mass Intensity\)](#) and/or [PMI-LCA \(Process Mass Intensity-Life Cycle Assessment\)](#).

Project Goal

Provide novel methods and/or strategies for improved solid phase peptide synthesis.

Project Timeline

It is expected that one year of research support will be sufficient to provide progress toward intended goals.

Proposal Format

Please be prepared to provide the following information in the application portal:

1. Name and email of grant officer
2. Name, title, phone, email and address of the Principal Investigator
3. Project Title
4. Research Group website
5. PDF of Proposed Plan of Work (*2 pages, 12 pt font, 1-inch margins*)
 - Objectives: Briefly state the project objectives
 - Project Approach: Include specific aims and investigations planned
 - Proposed milestone deliveries with brief description of the manner in which the researcher intends to achieve them
 - Brief description of the PI's research facilities and summary of the student's (undergraduate, graduate student and /or postdoc) capabilities to perform the proposed work
 - References (does not count toward your page limit)

Note: The PI should list any existing background intellectual property and/or collaborations they are aware of that might limit the freedom to operate any of the results arising from any research funded by ACS GCIPR. The priority of the Roundtable is to encourage research utilizing reaction conditions that are commercially available with the freedom to use.

6. PDF of Detailed Estimated Budget: The total amount requested would include all direct costs, student assistantships, etc. The total award is limited to \$80,000 for a grant period of up to 12 months.
 - Institutional overhead costs (indirect costs) should not be more than 10% of the total budget.
 - Post-doctoral associate salary and benefits are supported.
 - Student stipend and benefits are supported. Proposals for support of advanced graduate students are highly favored.
 - PI salary supplements will not be supported.
 - Laboratory supplies and instrument use charges are supported.
 - No funds may be allocated for travel, equipment purchase or repair, or administrative support.
7. Curriculum Vitae of Project Team Members: Please submit a curriculum vitae of each project team member (up to two pages per team member, combined into one document). This does not count toward your page limit.

Report Requirements

- Progress reports or updates are due monthly or bi-monthly from initiation of research and will be discussed in arranged web-conferences. Reports will be shared with the member companies of the Roundtable. A report template will be provided.

- Reports are to include research milestones/significant outcomes, summary of progress to date noting any deviations from the proposal, and research plans for upcoming months.
- A final comprehensive report is due one month after the end of the grant period. This report must be submitted as a PDF document electronically to gcipr@acs.org. In addition, the content of the report should be targeted for publication in a peer-reviewed technical journal. The paper will be co-authored by the principal investigator and student(s) performing the work with the guidance of member companies of the ACS GCIPR.

Intellectual Property, Publication Acknowledgement, and Terms of the Grant

- The primary purpose of this grant is the public dissemination of research through publication.
- Every patent, United States or foreign, that results from research funded (in part or in its entirety) by the ACS GCIPR Research Grant shall be immediately dedicated to the public, royalty free.
- Publication of results is expected within 6 months of work completion.
- Each publication prepared in connection with the ACS GCIPR Research Grant shall make acknowledgement in the following manner: “This manuscript was developed with the support of the American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable (www.acsgcipr.org). The ACS GCI is a non-profit organization whose mission is to catalyze and enable the implementation of green and sustainable chemistry throughout the global chemistry enterprise. The ACS GCI Pharmaceutical Roundtable, composed of pharmaceutical and related industries, was established in 2005 to encourage innovation while catalyzing the integration of green chemistry and green engineering in the pharmaceutical industry. The activities of the Roundtable reflect its member's shared belief that the pursuit of green chemistry and engineering is imperative for business and environmental sustainability.”
- Acceptance of a Roundtable Grant will be conditional upon agreement by the grantee institution that in the event the Principal Investigator is unable for any reason to conduct the research proposed, the funds, if previously paid by the Roundtable, shall, upon demand, be returned in full to the Roundtable, and further, that in the event the PI is unable for any reason to continue with the research after it has commenced, this grant shall be terminated forthwith and the unexpended and unencumbered balance of any funds theretofore advanced shall be returned to the Roundtable.
- The grantee institution, by acceptance of this grant, provides assurance that support normally provided by the institution for research of the faculty member will not be diminished.
- Applicants may have only one research grant with the ACS GCIPR at a time. In order to close a grant, the ACS GCIPR must receive and approve the required reports.

For additional information:

Website: www.acsgcipr.org

Email: gcipr@acs.org