Instructions & Information for Providers

Congratulations! You have been conditionally approved as a Provider for the BU-CMD compound repository.

> ***Final approval requires your Institution's signature on two non-negotiable Material Transfer Agreements: one to be executed between your institution and BU (PTA), and the other to be executed between your institution and any future Recipient(s) of your compounds (SPMTA).***

Please read the following instructions and guidelines carefully. In order to complete this submission, we need a number of items from you:

Part I: Compound Index

Please email the following to Lauren Brown (brownle@bu.edu)

- ✓ A final list of the compound(s) you intend to transfer, known as the **Compound Index**. This list should contain the structures of each individual molecule as a SMILES string, and unique Compound Identifiers. We cannot accept molecules that are not included in the Compound Index.

  When preparing this index, please be aware of the following:
  - *We cannot accept materials that are known to be corrosive, explosive, otherwise hazardous, or restricted/regulated by any government agency. Novel compounds of unknown hazard classification are acceptable, and will be handled by all recipients as if they are hazardous using prudent laboratory safety practices.*
  - *We reserve the right to reject compounds that are suspected by our team to be corrosive, highly water-reactive, or otherwise very hazardous (e.g. acyl chlorides, organic azides, etc.)*
  - *Our QC standards require that all compounds added to the collection be at least 90% pure by LC/MS with ELSD detection.*
  - *The 90% purity requirement extends to diastereomeric mixtures, and as such we cannot accept diastereomeric mixtures with less than 10:1 d.r.*
  - *We cannot accept compounds with multiple stereocenters, wherein the relative stereochemistry one or more stereocenters is undefined.*

Part II: Legal Agreements

After successful completion and review of Part I, we will circulate three-way MTA documents for your tech transfer office to review. After your TTO has indicated a willingness to sign and has provided the relevant contact details about your institution's signatory, we will circulate the following documents to all parties for signature using either AdobeSign or DocuSign:

- ✓ A signed, fully-executed **Provider Transfer Agreement (PTA)** between an authorized signatory at your institution and Boston University. This will enable the transfer of compounds from you to us as a repository.

- ✓ A signed, partially executed **Standard Provider Material Transfer Agreement Between Provider and Recipient (SPMTA)**. This partially executed document will be used with any future Recipient(s) of the compound(s) you deposit in our repository. A partially-executed copy of this Agreement will be held at BU. Each time a new Recipient signs on to receive your compounds, they will be required to execute the SPMTA that your institution previously executed, and you will be notified by receiving a copy of that fully-executed SPMTA via email.

Part III: Physical Compound Submission

Note: Compounds should be sent only **after** Parts I and II are fully complete!

Submission checklist (3 items):

- ✓ **5-25 mg of each compound** as dry powder/oil/film in a vessel that is indelibly labeled with a Compound Identifier.

  Note: A Compound Identifier is a name, number, or code that is linked back to your structure file. It is NOT a structure. Please do not draw structures on the vials or containers.

  - ➢ Each compound should be stable (or reasonably expected to be stable) and fully soluble in a 20 mM DMSO solution.

Note: DO NOT SEND DMSO SOLUTIONS. ONLY DRY POWDER/OILS/FILMS will be accepted.

- Each compound should exhibit >90% purity based on UPLC-MS-ELSD QC analysis, to be performed at BU on receipt.

  If our QC analysis fails, we will give you the opportunity to review and provide Supplementary Demonstration of composition and purity. Acceptable Supplementary Demonstration is:
  - Fully assigned ^{1}H and ^{13}C NMR spectra **plus**
  - Either high resolution mass spec **or** elemental analysis.

  Be prepared! Certain types of compounds including aldehydes, imines, poorly ionizable and low-molecular weight compounds are highly prone to poor behavior on reverse-phase UPLC-MS-ELSD. Be sure to have Supplementary Demonstration for these types of compounds ready prior to shipment, and do let us know if you suspect that there may be a QC issue with a compound in advance.

✓ **A single MSDS sheet** prepared for the set of compounds as a whole. We will provide you with a template for this document. Please do not send compounds you know to be corrosive, explosive, otherwise hazardous, or restricted/regulated by any government agency. We reserve the right to reject any compound(s) we suspect may fall under one of these categories.

✓ **Structure Information File.** This file can be either an Excel spreadsheet with SMILES strings, or an SDF file. All structures should be drawn according to our **Guidelines for Structure Drawing** specifications, which will be sent to you by email as a PDF. Each compound that you send should be annotated in the Structure Information file with fields containing the following:

- Information on the **quantity** of compound you are sending, in milligrams. Is this an accurate, measured amount, or just an estimate?

- Information on the **stereochemical composition** of each compound:
  - Whether each compound is **achiral**, **chiral racemic**, or **chiral enantioenriched**
  - If a scalemic mixture of enantiomers or a mixture of diastereomers is present, please provide the %ee and/or diastereomeric ratio. *Please note that to meet our purity threshold, diastereomeric ratios must be ≥ 10:1*

- Information on the **chemotype** of each compound:
  - Is the compound a named natural product? If so, kindly let us know the name of the natural product.

- **Is the compound an analog of a natural product (or natural product class)? If so, please let us know the name of the family of natural products that this molecule resembles.**
- **Have you published synthetic or other studies of this chemotype? If so, please provide the DOI for a pertinent publication.**

Preferred format for Structure Information File (either Excel spreadsheet with SMILES strings, or SDF file containing the fields below):

Structure (SDF) or SMILES (XLS)	Unique Compound Identifier	Amount (in mg)	Is this amount precisely weighed, or a rough estimate?	Stereochemical composition (achiral, chiral racemic, or chiral enantioenriched)	%ee and/or d.r. (if applicable)	Natural product name (if applicable)	Natural product family (if applicable)	Chemotype reference (DOI)

What to expect after submission:

When you send us your compounds, we will send you a confirmation email with your compound barcodes upon completion of the submission. Registered compounds will be included in all future distributions to our Chemical Library Consortium (CLC) network of Recipient screeners.

- The frequency and quantity of these distributions are irregular, and depend entirely on Recipient demand. We generally aim to provide "updates" of recent collection additions to our longstanding screening partners every 1-2 years. New screening partners are continually being added, and they will receive the full collection at the time that they join.

- If your compound is identified as a validated screening hit of interest to a biological collaborator, we will immediately notify you and put you in contact with the biologist who identified the activity. It is our hope that this will seed a future collaboration between you and the screening biologist, with or without BU-CMD involvement.

- At the BU-CMD, a hit is considered "validated" when its activity has been replicated with a freshly-QCed, resupplied aliquot of the sample. A large percentage of initial screening hits often do not validate for a variety of reasons. We may or may not contact you about unvalidated hits, depending mainly on the biologist's level of interest in the hit in question.

- If your compound is identified as a preliminary screening hit and we do not have material in adequate purity or quantity for a validation experiment, we will contact you to request a resupply.

- If you have not heard from us in a while, feel free to reach out. Even if your compounds have not hit in any screens, we will be able to provide you with some general information on where your compounds have been sent and what types of screens they have seen. Please note that due to bandwidth limitations, this information is currently only provided on request.

What we expect from you:

Our goal at the BU-CMD is to foster and enable scientific discoveries that seed new collaborations. Here are some short and simple "scientific etiquette" guidelines that we ask our network members to adhere to in order to keep collaborations running smoothly:

- When in doubt, don't show structures! (See more on this below)

- Our Depositors are not vendors, and our Recipients are not CROs. At the interface of chemistry and biology, the strongest and most productive collaborations are structured as an equal partnership between the chemists making molecules & the biologists studying them.

- Communication is key. Keep your collaborators well-informed of new developments and future plans that may impact them. Avoid making last-minute demands of a collaborator's time for proposals and publications – plan ahead!

- Aim to co-publish. In the current funding environment, grant applications with a successful collaborative track record (as evidenced by co-publications) have a higher likelihood of success. While our minimum publication expectation is that Recipients acknowledge Depositors & the BU-CMD as the source of materials, when a hit is discovered we strongly encourage structuring follow-on studies such that all parties may make author-level contributions to the published research.

Best practices in dealing with compound structures – an important note about disclosure

In the spirit of open scientific collaboration, we do not hold Depositors nor Recipients to any sort of confidentiality agreements. That said, we do make one strong but informal request: Please, **do not publicly disclose bioactive "hit" structures** without first consulting with the BU-CMD and the biological screener who identified the activity.

What constitutes public disclosure?

"Public disclosure" can include posters, papers, abstracts, theses, lectures, websites, etc. Even grant proposals, which can be subject to FOIA inquiry when funded, require special precautions for protecting IP-sensitive information.

Why is this important?

Premature public disclosure of the structures and activity of biologically active compounds can compromise our collective ability to publish and to patent promising drug leads, their derivatives and analogs.

I'm an advocate for Open Access science. Why should I care about patents?

It's certainly not unusual for a scientist to be more motivated by the potential impact of their research than its potential for profit. However, the unfortunate reality of drug discovery is that the two are intertwined. If a molecule is not properly IP-protected, it is likely not going to be developable as a drug. In order to maximize potential for your research to meaningfully impact those who suffer from disease, we are obligated to take adequate precautions around IP for molecule classes that have therapeutic potential.

How should we move forward when a hit is identified?

The BU-CMD will work collectively with Depositors and Recipients to determine a responsible and appropriate path forward that adequately balances our dual (and sometimes dueling) obligations to promptly publish our results while protecting the IP of promising drug leads. In general, it is up to the parties' institutions to make final decisions on patent filings, with inventorship determined in accordance with US patent law.