FAQs for the Metabolomics Program Stage II FOAs:

| RFA-RM-17-011 | National Metabolomics Data Repository |
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| RFA-RM-17-012 | Metabolomic Data Analysis and Interpretation Tools |
| RFA-RM-17-013 | Compound Identification Development Cores |
| RFA-RM-17-014 | Stakeholder Engagement and Program Coordination Center |

Part I: General Questions

1. Will there be a webinar recording available?

No, we feel that the slides available on the Common Fund Metabolomics Program website and these FAQs will be more useful than a webinar recording. The slides and FAQs can be accessed from this page: https://commonfund.nih.gov/metabolomics/webinars.

2. Are foreign institutions eligible to apply?

Foreign institutions are not eligible to submit applications in response to these RFAs, however foreign collaborators are allowed, so there can be sub-contracts to foreign institutions and the multi-component awards can have foreign components.

3. Are these RFAs being issued for just a single award cycle, or will there be similar announcements made later?

These are single receipt date RFAs. There are no plans to re-issue them again later.

4. Are cross-institutional collaborations favored for any of these RFAs?

There is no requirement or preference for cross-institutional collaborations. Collaborator choice should be scientifically justified in the application, along with the collaborator's qualifications.

5. Will grantees from the four RFAs be coordinated under one consortium?

Yes, there will a Common Fund Metabolomics Consortium which will involve investigators from all of these initiatives. Cooperation among grantees strengths the overall program. Please read cooperative agreement terms carefully.

6. Can the same PI submit multiple applications, either to the same RFA or to multiple RFAs?

There is no limit to the number of applications an investigator may submit, either in response to the same RFA or to different RFAs. However, each application must be scientifically distinct. Final funding decisions will take into consideration the goal of having broad representation of investigators in the consortium.

7. How many annual consortium meetings should be included in the budget?

Each year, there will be an Annual Investigators' Meeting, which will be approximately 2 days long and will be held domestically. There will also be one additional in-person Steering Committee meeting, for the PD/PIs only, which will be 1-2 days and also held domestically. Please budget accordingly.

Part II: Questions Pertaining to RFA-RM-17-011 National Metabolomics Data Repository

8. Should the NMDR application propose development of data analysis tools?

The purpose of the National Repository is for storage of and access to datasets with appropriate metadata and protocols so they can be reviewed and reanalyzed by the community at large. Any tools developed by the Data Repository should lower the effort associated with data deposition and retrieval in accordance with the FAIR principle.

9. Will data from the current DRCC Metabolomics Workbench be incorporated in the NMDR Data Repository?

All data currently found in the DRCC Data Repository will be available through the NMDR database.

Part III: Questions Pertaining to RFA-RM-17-012 Metabolomic Data Analysis and Interpretation Tools

10. Do applications submitted in response to this RFA need to focus on a single area listed or can they address multiple areas from the list?

Applications can address one or more areas listed in the RFA.

11. Does this RFA cover development of new tools or extended development of existing tools? Tools should address a defined roadblock(s) in metabolomics data analysis. This could include the development of new tools or extended development of existing tools. Applicants should describe the need that is being addressed by the application, and justify the responsiveness to the RFA.

12. Does this RFA support the generation of data?

The goal of the RFA is to build data analysis tools using existing metabolomics data from collaborators or found in a data repository. The RFA was not intended to support the generation of primary metabolomics data. In the specific scenario where existing data is not appropriate for testing the tool, funds for generation of appropriate data may be included, but a strong justification for why existing data would not be appropriate is necessary.

13. If applicants should use existing data, why does the RFA require collaboration with a metabolomics researcher?

The goal of the RFA is to generate analytical tools to best address current data analysis issues in the metabolomics field. A collaborator with metabolomics expertise is needed in order to provide input regarding the data analysis needs of the metabolomics community and validate the utility of developed tools for the intended audience.

- 14. Can the PI of a data analysis application also serve as the required metabolomics researcher?

 Yes, the PI of a data analysis application can also serve as the metabolomics researcher if he/she has appropriate metabolomics expertise.
- **15.** Does NIH want applicants to this RFA to collaborate with an existing metabolomics center? No, collaboration with an existing metabolomics center is not required.
- 16. Would development of an online data processing service be responsive the RFA?

While an online data processing service may address a need in the metabolomics field, and could be relevant to one or more of the specific areas of research interests listed in the RFA, applications in response to this RFA are expected to develop a tool or approach that is portable and endures beyond the funded project period.

- 17. Would database curation fit within the scope of this effort?
 - Curation of various metabolomics reference databases used in metabolomics data analyses could be justified as fitting within at least one of the areas listed. Curation of specific metabolomics datasets would not be responsive. As with any research topic, it's incumbent on the applicant to describe the need and justify its fit with the RFA.
- 18. Would development of a resource/pipeline, that uses existing analytical tools but allows investigators to choose the tool they want to use, be appropriate for this RFA? Applications should address one of the defined areas of research interest identified in the RFA. An umbrella resource for selection of existing tools is not one of the defined areas.
- 19. As the goal of the RFA is to stimulate development of tools that are accessible to a broader audience of scientists, will it be critical that these grants include the development of GUI software tools, rather than just developing software that can be accessed through use of a programming language (for example, R packages)?
 We expect the interface to be appropriate for the intended users. If the development of GUI software tools allows use by the broader biomedical community, then it would be a strength.
- 20. Will the composition of the grant review panel be mostly people with technical expertise in data analysis tool development, or will it be a broader panel that includes scientists without programming expertise?

 The review panel will be recruited to reflect the appropriate expertise needed to review the
 - The review panel will be recruited to reflect the appropriate expertise needed to review the applications submitted.
- 21. How extensive (and what types) of preliminary data are expected for the proposal?

 Some applicants may have preliminary data on early stage or extended tool development. For novel tool development, there may not be preliminary data on the actual development of the tool. At minimum, applicants should have a history of data analysis tool development and describe how that history relates to the tool proposed, including how previous tool(s) were disseminated and what impact the tool(s) had. Also, the applicant should demonstrate the need for the proposed tool, i.e. what capability will it provide and who will use it.

Part IV: Questions Pertaining to RFA-RM-17-013 Compound Identification Development Cores (CIDCs)

22. Is a project focused on identifying the unknowns in a given experiment appropriate to this program?

Superficially no, the focus of the CIDC program is to develop the capability to identify 'unknown' features in untargeted metabolomics analyses. Mining of existing data sets, or validation of models in a defined biological area are appropriate but should not be the central focus of an application. Methods should be developed to be more generalizable – we want to catalyze the field, not just resolve one experiment.

23. Do compound identification efforts need to focus on compounds found in human samples?

Since the goal of the RFA is the development of compound identification methods, the sample is largely irrelevant. However, the applicant should justify why the proposed samples are being used and how methods developed through those samples will be broadly useful for biomedically relevant compounds.

- **24.** Is there a defined balance between the Computational Core and the Experimental Core?

 No, both are required elements but applicants have the freedom to define the balance and interactions between these Cores as part of the design and structure of the proposed Core.
- 25. Is a Computational Core required, or allowed, to develop software packages?

 The focus of the Computational Core is the development of approaches, including *in silico* approaches, to facilitate the identification of unknowns. The end-product may be a complete software package, but this is not required. The development of software for data analysis as a central focus is more appropriate for RFA-RM-17-012, but note that compound identification is excluded from that initiative.
- 26. Is the Experimental Core intended to focus on the development of experimental methodologies for compound identification or on the validation of models developed in the Computational Core?

Either approach, or a combination, may be appropriate provided that the overall focus of the Center is to develop methods, models, and technologies for compound identification.

27. Do the compound ID cores need to be service-oriented?

The intent of the Compound Identification Cores is to develop methods and tools to enable compound identification on a large scale and address the barrier of frequent 'unknown' hits in untargeted metabolomics studies. The Cores are not intended to serve as service facilities supporting compound identification for the broad community.

28. Does this initiative provide funds for capital instrumentation costs?

These costs are allowable with strong justification. However, applicants are encouraged to focus on the scientific goals of the RFA, rather than on expanding equipment or infrastructure.

29. If a research team has sufficient computational capability to generate *in silico* reference data for broad expanses of chemical space, then is there a need to have a described strategy for focusing on certain molecules?

Applicants are not required to focus the project on a subset of chemical space. However, applications must include a plan to experimentally validate computational predictions, and applicants will need to select specific chemical classes for validation experiments. The rationale for those selections should include the biomedical relevance of the chemical classes chosen for validation.

Part V: Questions Pertaining to RFA-RM-17-014 Stakeholder Engagement and Program Coordination Center

30. Please clarify the distinction between activities of NMDR and SEPCC. For instance, whose responsibility is the web portal to access the data?

Applicants for each initiative should focus on the core goals of the specific RFA. The goals of the NMDR are related to metabolomics data: Data deposition, data storage and maintenance, data access and retrieval. In contrast, the goals of the SEPCC are related to program coordination, outreach, consensus building, and dissemination. This includes maintaining and providing access to and ensuring usability of Consortium resources, which includes the data repository. What this means is that the SEPCC and the NMDR will need to work closely together. We envision that the Data Repository itself will be maintained by the NMDR but that it will be accessed through the web portal developed and maintained by SEPCC. Similarly, testing usability of the Repository will require collaboration between the SEPCC and the NMDR.

31. Can you provide examples of stakeholder communities that would be relevant for the SEPCC outreach effort?

Relevant communities are listed in the FOA and could include (but are not limited to) national and international metabolomics researchers, large existing NIH-funded projects or consortia that use metabolomics, researchers in related fields, the greater biomedical research community, professional societies, journal editors, and industry partners.