



COMETS (Consortium of METabolomics Studies)

BYLAWS

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I. Mission

The COMETS Mission is to promote collaborations among prospective cohort studies that follow participants for a range of outcomes and perform metabolomic profiling of individuals. COMETS aims to facilitate an open exchange of ideas, knowledge, and results to accelerate a shared goal of studying the metabolomic profiles associated with chronic disease phenotypes (e.g., heart disease, diabetes, cancer).

Within the scope defined by its Mission, the objectives of COMETS are to:

1. Provide a framework to foster international collaborations among studies sharing common objectives;
2. Provide a forum for the discussion, development, and pursuit of new collaborative studies and research directions;
3. Support the development of early career researchers; and
4. Advance the knowledge of the metabolome to improve our understanding of prediction of disease etiology, diagnosis, and prognosis.

II. Membership Eligibility Criteria

Cohort eligibility criteria

At present, eligibility is restricted to cohorts with measured metabolomic profiles in blood using either mass spectrometry or nuclear magnetic resonance spectroscopy in at least 100 participants with follow-up for disease incidence. As the technology advances and the COMETS consortium matures, this stipulation is open to modification. Membership is granted upon majority vote of the Executive Committee (EC).

Consortium membership falls under the three (3) categories below. Individuals who are interested in Consortium membership and are not members of the EC will follow the guidelines and eligibility under Steering Committee (SC) and Consortium Members (CM) membership.

Categories of Membership

*Executive Committee (EC) Member**

There are twelve (12) elected EC members. The EC coordinates COMETS policies and guidelines, approves membership and project proposal requests, serves to facilitate scientific progress through assisting with the planning and development of collaborative consortium activities and with cross-Consortium communications, and assists in the resolution of procedural disputes among members. To achieve these functions, the EC maintains the voting rights of the consortium [one (1) vote per EC member]. The EC is responsible to and elected by the SC members of COMETS for those aforementioned purposes.

Steering Committee (SC) Member*

SC members are the primary representatives of the participating studies [one (1) per cohort as appointed by the cohort] and are entitled to vote for the election of EC members. SC members advise the EC on all consortium matters. They review project proposals, participate in interest groups (IG) and can become IG chairs. Membership is effective upon notification and confirmation of acceptance of the cohort application by the current EC.

Consortium Members (CM) Member

CM members are investigators who are working in the field of metabolomics. Membership requires a nomination by an EC or SC member and is effective upon acceptance by the EC. CM members are required to maintain active participation in at least one IG and may become IG chairs. CM members do not have voting rights.

*If an SC member is elected to the EC, the EC member continues in his/her role as representative for the cohort. Another SC member will not be appointed.

Selection of the Steering Committee, Officers, and Proposal Review Chair

The following principles shall guide the composition, nominations, elections, terms of service, and removal for elected positions in COMETS:

Composition

1. There are twelve (12) elected EC members. An additional EC member, specifically an NCI extramural program staff member from the Division of Cancer Control and Population Sciences, is nominated by the NCI so that the EC totals thirteen (13) representatives.
2. There are three (3) elected Officers (Chair, Vice-Chair, and Secretary). These officers also serve on the EC and constitute three (3) of its twelve (12) elected members.
3. There is one (1) Proposal Review Chair. This person shall be a volunteer from among the nine (9) elected EC members not currently serving as an Officer. If multiple individuals volunteer, the Officers will select the Proposal Review Chair from among them.
4. EC members and Officers are elected by vote of the SC (see *Nominations and Elections* below). Members should consider balanced representation when nominating persons for an upcoming election. The EC members and Officers should reflect the diversity of expertise, institutions, gender, and geographic regions of the COMETS membership as much as possible given COMETS members available to serve.

Nominations and elections

1. At the end of each calendar year, one Officer and several EC members will retire (see *Terms of Service*), thus creating new open positions for the next calendar year.
2. Nominations for these positions are called by the end of February and close by the end of March.
3. SC members who are not currently serving on the EC are eligible to be nominated for the EC. Only current COMETS EC members can be nominated for an Officer position. Officers may not be nominated for other Officer positions.
4. All nominations must be accompanied by a brief paragraph describing the nominee's contribution and participation in COMETS and a statement describing the contribution he/she hopes to make in serving on the EC or as an Officer. Nominations are submitted to the Secretary and compiled for review by the standing EC. All COMETS nominees are contacted by the Chair of the standing EC to confirm their interest in being included on an election ballot prior to the circulation of the ballots. At the close of nominations, each candidate's name, institution, affiliated study, geographic region and statement of contribution and future direction will be circulated and/or posted to the web portal.
5. Elections will be conducted through e-mail or portal-based ballot. A voting member of COMETS is a member of the SC. Each participating cohort has one representative on the SC and one vote. Each SC member is given the opportunity to complete one ballot or survey (i.e., via e-mail or the web portal) and scores the four (4) candidates of their choice as first preference (score of 4), second preference (score of 3), third preference (score of 2) and fourth preference (score of 1). The nominees with the highest scores will be appointed to the EC. If there is a tie, the appointment goes to the nominee with the highest number of first preference. The closing date for receipt of members' votes will be mid-April. The Secretary will receive and tabulate the votes to preserve anonymity and vote tallies will remain confidential. Results will be announced by e-mail and posted on the portal as soon as possible and no later than May 1.
6. For the first year, special rules will apply to ensure that retirements are balanced across calendar years, as follows:
 - a. The three Officers serving at the time these Bylaws were adopted will have 0, 1, and 2 years of remaining service. That is, the Officer with the most years of service will retire at the end of 2021, the Officer with the second-most years of service will retire at the end of 2022, and the remaining Officer will retire at the end of 2023.
 - b. One Officer and nine (9) non-Officer EC positions will thus be open for nominations in the first year. If only one person is nominated for each available position, they are declared elected. If more than one person is nominated for a position, there will be an election and the highest-scoring candidates will be declared elected. All candidates for Officer will also be considered as candidates for EC.
 - c. The EC members elected in the first year will make their first item of business to randomly assign who will retire in years 1, 2, and 3 (e.g. "pull names from a hat"). Three members will be assigned to retire each year. Per below, subsequent election to Officer would initiate a new term of service that supersedes these assignments.

Terms of service

1. The term of service for each position is three (3) years and begins on June 1 following the elections. Election to an Officer position initiates a new three (3)-year term of service on the EC for these individuals. These individuals will therefore serve a minimum of four (4) years on the EC.
2. EC members who have served the duration of their term and were not elected to an Officer position will retire at the end of the calendar year.
3. Officers who have served the duration of their term will retire at the end of the calendar year.
4. Any retired EC member may be re-nominated for the EC after a one (1)-year break in their EC membership. This person becomes eligible again for elections for the EC.
5. If an EC member steps down from their position prior to the end of their term, a special election will be held to replace the EC member. The newly elected EC member will fulfill the remaining term for the EC member that they are replacing.

III. Officers: Chair, Vice-Chair, and Secretary

Chair

The Chair is a member of the EC and provides leadership to the members of the consortium. He/she is responsible for chairing the meetings and conference calls of the EC and SC after developing the agenda in consultation with the Vice-Chair, Secretary, and NCI Program staff. Additionally, the Chair is responsible for assuring that action items and tasks identified during EC and SC meetings and conference calls are completed in a timely fashion.

Vice-Chair

The Vice-Chair is a member of the EC, and he/she works closely with the Chair to develop EC meeting and conference call agendas. The Vice-Chair also performs other responsibilities as assigned by the EC. The Vice-Chair performs Chair responsibilities (see above) when the Chair cannot be available. The Vice-Chair automatically assumes the duties of the Chair if the Chair becomes indisposed.

Secretary

The Secretary is a member of the EC. He/she works closely with the Chair and Vice-Chair to develop EC meeting and conference call agendas, maintains records of the EC, ensures effective management of consortium records, manages the minutes of EC and member meetings, and ensures that the minutes are distributed to the EC and members (as determined by the EC) shortly after each meeting. Additionally, the Secretary is sufficiently familiar with consortium policies to note applicability during meetings.

Proposal Review Chair

The Proposal Review Chair will be selected from the EC and will serve a three (3)-year term in this position. The duties of the Proposal Review Chair will be to:

1. Keep the deadlines for submission updated on the COMETS website.
2. For each round of review:
 - a. Set up a conference call for review of the proposals.
 - b. Send the proposals to all EC and SC members and solicit comments.
 - c. Assign a primary reviewer from the EC or SC for each of the proposals.

- d. Run the review conference call.
 - e. Send revised proposals to the EC and get final vote.
3. For approved proposals from trainees, identify an EC or SC mentor and connect that individual with the trainee.

If the proposal review chair becomes an officer or resigns before the end of their term, a replacement will be selected from EC volunteers. The replacement will serve the remainder of the term.

IV. Executive Committee Meeting Quorum

Attendance of nine (9) members constitutes a quorum to call an official meeting of the EC. Voting may only take place at an official meeting where a quorum is present.

V. Interest Group (IG) Policies

IG Definition and Activities

IGs consist of COMETS investigators, fellows, and other researchers interested in a particular research topic.

IG activities may include, but are not limited to:

1. Evaluating gaps in the literature and research needs for the topic of interest;
2. Standardizing exposure/endpoint data across cohorts as needed for projects;
3. Coordinating/conducting the research project and/or drafting manuscripts;
4. Determining whether additional follow-up work or studies are needed, such as in confirmation samples.

Process for Establishing IGs

To initiate a new IG, an investigator should complete the new IG application form. This form will ask the investigator to provide his or her name, a name for the group, a working draft of the mission and objectives of that group, and specify the working group type (i.e. permanent, ad hoc). This form is different from that of the project proposal that outlines the details of one particular project.

IGs are then discussed by the EC and established by a majority vote. Any interested COMETS member may join an established permanent IG. Cohorts may join individual projects, and if they lead to a publication, be entitled to appropriate authorship under the COMETS authorship guidelines. Cohorts contributing data should have a defined point person to contact for questions about data and other issues.

Upon establishing an IG, the EC appoints a Coordinator to convene the first IG conference call or meeting. At this first session, the IG may select its own Chair or Co-Chairs to arrange, coordinate, and run the meetings and calls. The Chair or Co-Chairs may or may not be the Coordinator originally identified by the EC.

Changing Chairs and Dissolving the Interest Group

The interest group determines how they would like to proceed with the length of term of its Chair, which can be a regular rotation (e.g. elect a new chair yearly or Chairs step down after they have completed a significant project that they are leading, etc.).

The Chairs and IG determine when the working group should be dissolved. However, if the EC determines that a working group has been inactive for a significant period (e.g. one year), they too may recommend dissolving a particular IG.

Ad Hoc Interest Group

We anticipate that specific needs, topics, tasks, and objectives identified by COMETS consortium members will necessitate the establishment of an ad hoc IG, that is a temporary working group with a defined mission or objective that will meet the needs of consortium members. Ad hoc IG can be proposed by any COMETS member and will be established upon the agreement of the EC using the same protocol as a permanent interest group. Each ad hoc IG will have a defined mission that is brought to the EC for approval. The ad hoc IG will specify a regular meeting structure that is in line with the specified mission of the group. Once approved by the EC, the ad hoc IG will meet on a regular basis as agreed upon until the objective is achieved. Upon completion of the specified objective(s), the ad hoc IG will dissolve. There may be instances when an ad hoc IG is developed with a specific objective that fits within a larger, permanent IG. In this case, the ad hoc IG may work in conjunction larger IG with relevant interests. Ad hoc IGs may require permission of the IG Chair to join.

VI. COMETS Project Proposals

Proposal Project Process

COMETS projects can be data-driven analyses, methods development projects, or surveys that use data requested from prospective cohorts that are participating in COMETS.

Project proposals are first submitted by an investigator to the Proposal Review Chair using the approved submission form. The project proposal will describe the proposed analysis, specific outcomes, name(s) of lead investigator(s), and the proposed timeline. Proposals should be narrow in scope and highly focused.

Review Process

The project proposal is next submitted to the SC, which will determine whether the proposal is unique—i.e., not duplicative of other COMETS efforts—and whether the proposal is appropriately narrow in scope and provide a preliminary vote. The proposal review chair will assign a primary reviewer from the EC or SC who will present the proposal and lead the discussion of it on a conference call specifically to review proposals which all proposers and SC and EC members are invited to attend. The proposer will revise the proposal as requested on the call as needed and submit the revised proposal to the proposal review chair. The final vote will be done by the EC with the majority score determining the approval. For approved proposals, the investigators will circulate the proposal to all COMETS members, who will be allowed to “opt in” to the project. For proposals requiring additional revisions, the proposers will be allowed to submit additional revisions to the EC, which will have additional votes on the proposal as needed. Rejected proposal can be resubmitted in the next round.

For submitters who are currently in training positions (graduate student or postdoctoral fellow), a letter supporting the proposal must be submitted with the proposal by the submitter's institutional mentor. In addition, a sponsor must be identified for the proposal. The sponsor must be an active EC or SC member and identifying a sponsor can be achieved in one of two ways:

1. If the trainee is affiliated with a participating cohort and working with an EC or SC member, he/she may indicate the sponsor at the time of submission on the proposal form.
2. If a submitter is not affiliated with a participating cohort, and therefore not directly working with an EC or SC member, the proposal review chair will identify a sponsor for the project upon approval of the proposal.

For approved proposals, each cohort that "opts in" will designate an investigator to be the primary representative for his or her cohort. The primary cohort representative will inform the lead investigator on the project proposal that he/she is the designated representative for the project. These representatives, along with the Principal Investigator and other investigators actively involved in the project, will be designated as the Project Proposal Group (PPG).

Progress Reports for Approved COMETS Proposals

1. Progress will be reported annually (as defined under item 4) on February 1st.
2. Any proposal for which no progress has been made for two consecutive years will be discontinued unless extenuating circumstances (as defined under item 5) can be demonstrated.
3. Proposals for which analyses have not begun within 3 years of approval will be discontinued unless extenuating circumstances (as defined under item 5) can be demonstrated.
4. Progress could include recruitment of cohorts, development of a working group, development of statistical models, preparation, and submission of grants to fund proposed project, data analysis and manuscript preparation.
5. Extenuating circumstances could include waiting for results of a grant review or a functionality update in COMETS analytics, disruption of funding and/or research because of change of institution, or proposal is dependent on data from another project that is not yet available.

VII. Principles for Analyses Based on Aggregate Results Sharing

Overall Guiding Principles

A major goal of COMETS is to produce jointly coordinated, multicohort, high-impact publications describing relationships between metabolites and diseases (e.g., diabetes, cardiovascular disease, cancer), and other biological constructs (e.g., aging, genetics).

Many, though not necessarily all, analyses will be done through aggregate results sharing. Aggregate results sharing is a process in which data analysis occurs separately within each participating cohort, then the results are shared so that they can be meta-analyzed.

Aggregate results do not include individual-level data; separate agreements would be needed for sharing of individual-level data.

These guidelines establish agreed-upon protocols meant to encourage investigators to conduct their research in the spirit of collaboration and trust.

Definition and Timing of Opt-in for Manuscripts

Cohorts will share aggregate results and the guidelines for “opt-in” depend on whether data sharing has occurred. These guidelines do not preclude cohorts from publishing their own study-specific data although cohorts should communicate any related plans to the COMETS PPG.

Post-proposal but pre-data sharing

1. The decision to “opt in” to an analysis occurs after submission of the COMETS Project Proposal. The “opt-in” represents a commitment to collaborate only with the COMETS PPG and no other consortia-based groups for the analysis described in the project proposal.
2. Cohort representatives have the option to “opt out” any time before formal distribution of shared results (see *Primary Results Distribution* below). Prior to distribution of shared results, the lead investigator will prepare a detailed data analysis plan that is reviewed by PPG members. The plan will include a timeline and target dates for completing analyses, sharing aggregate results, conducting additional analyses, and submitting the manuscript to a journal.

Post data-sharing

1. Sometimes, a few of the participating cohorts may, for various reasons and/or despite their best efforts, be unable to complete their metabolomics analyses on time. To ensure timely publication, PIs may determine that data sharing and preliminary meta-analysis can occur between two or more participating cohorts given the parameters defined for data sharing for a manuscript. This is at the discretion of the PPG.
2. Once the first draft of the manuscript is circulated, no cohort that has “opted in” may then “opt out” of the manuscript.

Primary Results Distribution (Prior to Publication)

1. Cohort-specific aggregate results will be submitted to the lead investigator or analyst via a secure website. Results will be submitted in a standard format agreed upon in advance by the lead investigator and cohort representatives. The shared files will include a complete listing of aggregate association results for all metabolites present within the data set and appropriate documentation (as determined by the lead investigator).
2. Submission of prepublication results, such as in an abstract or grant application, must be agreed upon by all cohort representatives and be consistent with the initial COMETS Project Proposal. The results and draft abstract should be submitted to cohort representatives at least 7 days in advance of the abstract guideline.
3. Secondary distribution of unpublished COMETS aggregate results to investigators or other persons who have not explicitly “opted in” to the COMETS Project Proposal may occur only after approval by the PPG and confirmation by the COMETS EC. In general, such secondary distribution will be discouraged until after the relevant manuscript has been accepted for publication. If the secondary distribution of unpublished results is

- approved to occur prior the manuscript being published, a data transfer agreement should be in place between the parties sharing and receiving the data.
4. All involved investigators/cohort representatives agree to keep the other investigators in the PPG informed about additional analyses and follow-up experiment plans related to the approved COMETS project proposal.
 5. During the pre-publication period, any sharing of aggregate results not stipulated in the bylaws is not allowed unless the issue is brought to the COMETS EC for discussion and approval.
 6. The consortium expects that the data will be used for legitimate research purposes and requests that users of the data acknowledge the appropriate consortium investigators for their work.
 7. For manuscripts, PPG members ensure that any necessary disclaimers, reviews, and approvals on behalf of the parent studies take place as required. These approvals should occur within one (1) month of the completion of the final draft unless extenuating circumstances are documented.

VIII. Authorship Policy

General Principles

The approach to authorship will be inclusive rather than exclusive, although authors should meet the criteria proposed by the International Committee of Medical Journal Editors (ICMJE) (Annals of Int Med 1988;258-304). The ICMJE specified that authorship credit should be limited to those who contribute substantially to all of the following:

- Conception and design, or acquisition of data, or analysis and interpretation of data;
- Drafting the article or revising it critically for important intellectual content; and
- Final approval of the version to be published.

For each project, authorship is agreed upon as it is initiated and revisited during the manuscript stage to ensure that it reflects this agreement and policy prior to submission.

Authorship Guidelines and Policies

General Format for Authorship: Writing and Analysis Team (defined below) lead(s), data coauthors in alphabetical order, Writing and Analysis Team senior author(s)

The author list will begin with the members of the Writing and Analysis Team (except the senior author(s)). Data coauthors will be listed in alphabetical order after the Writing and Analysis Team. The last author(s) will be the senior researcher(s) responsible for that particular manuscript/project.

Writing and Analysis Team

Manuscripts typically will be led by a writing group that consists of a small number of consortium members. The person who submitted the proposal will assemble the Writing and Analysis Team from among those who express interest, spreading membership across cohorts as much as possible. All Writing and Analysis Team members are expected to advise on data analysis, assist in interpreting results, and provide in-depth reading and feedback on drafts prior to circulation to the whole group.

Members of this group rightfully will claim slots at the front and back end of the paper as outlined below, with the specific location determined by contribution and internal discussion among the members. In general, the following definitions should be applied when determining these key authorship slots:

- *Lead Author(s)*: These are the researcher(s) on the Writing and Analysis Team who will take primary responsibility for data analysis and writing and will be considered first authors.
- *Senior Author(s)*: These are the researcher(s) who submitted the proposal or are mentors of the person who submitted the proposal. Their role is to edit the paper and accept full responsibility for its content.
- *Other Writing and Analysis Team Member(s)*: These are the researcher(s) who comprised part of the Writing and Analysis Team but do not meet the definitions of a lead or senior author. The order of authorship for these members will be determined based on their contribution to the Writing and Analysis Team but should be grouped just before the data coauthors.

Other important authorship principles for the Writing and Analysis Team include:

- All consortium members, including members who are not contributing primary data, are eligible to participate in writing groups.
- Either the lead or senior investigator will serve as the corresponding author. Multiple corresponding authorship is encouraged.
- Early-career investigators are encouraged to lead projects and, as such, lead in authorship.
- Multiple co-first and co-last authors are permitted to recognize equal efforts and contributions among writing group members. If the journal permits it, the writing group and co-first or co-last authors should be specified in a footnote.
- If major imbalances appear between cohorts, and if these imbalances do not fairly reflect the level of contribution, the authorship lists will be negotiated with the EC (see Section VIII).
- Cohort representatives are not required to participate in a Writing and Analysis Team to be a coauthor (see Data Coauthors, below).

Data Coauthors

Members of groups that contribute data to a collaborative project will be recognized as coauthors. (Preference should be given to the person who facilitated the analysis, responded to questions, and reviewed the work as it progressed—at the discretion of the project Principal Investigator [PI]). Each cohort will be permitted a specified number of authors depending on the sample size that is contributed to the approved project proposal. Each cohort will be permitted to have a minimum of two (2) data coauthors up to a maximum of six (6) data coauthors. The sample size threshold scheme for number of data coauthors is below:

<5000 samples = 2 authors
5000 – 9999 = 3 authors
10000 – 14999 = 4 authors
15000 – 19999 = 5 authors

20000+ samples = 6 authors (maximum)

IX. Dispute Resolution

If any disputes between consortium members arise (e.g. project approval, authorship, participation in projects, etc.), the member should first address the concerns individually with the other COMETS member to reach a resolution. If no resolution is met, a member may request that the EC review the circumstances. For the EC to review the circumstances, the request must be put in writing to the EC for review and submitted 7 days prior to the monthly EC meeting. The EC will review the request and determine next steps by majority vote. Once the EC has determined next steps, they may request additional information from relevant consortium members. Based on all information, the EC will determine how to resolve the dispute. This decision is final.

X. Removals

SC or EC members may be removed for cause, such as violating the bylaws, scientific misconduct, etc., by majority vote of all SC members present at any regular meeting of the SC plus all SC members who respond via electronic means who were not present at the regular meeting provided that a statement of the reason or reasons shall have been e-mailed to the member being considered for removal at least fourteen (14) days before any final action is taken by consortium members. This statement shall be accompanied by a notice of the time when, and the meeting at which, the consortium is to act on the removal. The member shall be given an opportunity to be heard and the matter considered by the consortium at the time and place mentioned in the notice. At the completion of the process, the decision of the SC is final and cannot be appealed.

XI. Amendments

These Bylaws, or any provision hereof, may be amended or repealed either by the affirmative vote of one-half (1/2) of the members present at any meeting of SC (in person or via electronic means), provided that the substance or effect of the proposed amendment or repeal has been stated in the notice of such meeting.

XII. General Expectations

The consortium is for the exchange of ideas, knowledge, and data/aggregate results in metabolomics studies. To maintain this focus on scientific collaboration, members will not use the consortium as a vehicle to sell or promote products or services.

Cohorts that join COMETS will commit to sharing basic cohort details and to allowing these details to be made public, such as through the COMETS website or COMETS metabolite dictionary. Details of interest include the number of participants with metabolomics data, the participant demographics, the names of the specific metabolites measured, and the method by which metabolites were measured. Researchers planning new COMETS projects and publishing COMETS papers vitally depend on such information being publicly available.

All members of COMETS are expected to abide by the COMETS bylaws.