

Guidelines for Approach Section of CIDR Applications

The guidelines below are based on advice from members of the CIDR Access Committee. They summarize the key information that reviewers want to see in your CIDR application and the preferred presentation format. When composing the Approach section, please provide ALL of the information requested below and use the heading provided below in bold.

Please note that the application as a whole should reflect the commitment and involvement of the key personnel for the genotyping effort, including the genetic analyst. If you are not the statistical analyst for your project, it is important to get that person involved as early as possible both in the design of the project and in the CIDR application itself.

Approach:

Sample Information: Provide a table with a clear description of sample numbers, DNA source (tissue), and the requested CIDR service. An example is shown below.

Sample Set (include reference name, case/control status if relevant)	Number of Samples	DNA Source	Service Requested
ABC cases	1,000	blood	HumanOmni1-Quad
DEF cases	750	n/a, already genotyped	(genotyped with Human1M-Duo)
ABC controls	1,200	blood	HumanOmni1-Quad
DEF controls	500	n/a, already genotyped	(genotyped with Human1M-Duo)
Follow Up: ACB sample cases	3,000	saliva	3,072 Custom SNPs
Follow Up: ACB population controls	3,000	saliva	3,072 Custom SNPs

If subjects were collected from multiple sites, this should be clearly indicated on the table. If it enhances clarity, list each sample group in a separate row in the table. If there are additional subjects who have already been genotyped (or are currently being genotyped elsewhere) that will be included in the analysis, include that information in the table. In your supporting documentation, provide evidence that you have access to these data.

Provide supporting text describing relevant detail about the origin and phenotype of the subjects. Also describe the extraction methods used for each DNA source and the approximate DNA concentrations. Include information about any previous genotyping that has been done on the samples to be typed at CIDR. Indicate when the samples will be ready to ship to CIDR.

Description of Disease/Trait: Include detailed information about the phenotypic characterization of the subjects and describe any relevant endophenotypes or secondary phenotypes that have been measured. Describe relevant environmental factors that have been measured. Summarize the what is know about heritability and transmission of the disease/trait and how that supports the choices made for the requested study.

Study Population: Describe the study population and the method of selection. For case-control studies, provide specific inclusion and exclusion criteria for cases and controls. If applicable, describe how cases were identified and sampled, whether controls were matched to cases, and if so, how they were matched and how effective the matching has been. For trios and families define how offspring were selected and the completeness of pedigrees. Indicate whether parentage was confirmed by genotyping. Describe any special features of the population that would enhance its value for the study proposed. For mouse studies, provide reasons for strain choices.

Justification of Services Requested: Provide a clear justification for the particular service requested. For GWAS, include a justification for a GWAS study design. Also provide the justification for the array chosen and why other genotyping arrays are less appropriate. For custom SNP projects, include a justification for the choice of service and number of SNPs requested.

Power and Effect Size: Using power analyses, describe the range of effect sizes detectable by the study. In the analyses address relevant features of the analytic plan, such as genetic models to be tested, the extent of multiple testing, and what significance level would be used for testing; important parameters such as risk allele frequencies; as well as expected patterns of linkage disequilibrium. If the study design requires separate analysis of groups of subjects (e.g., phenotypic classes or ancestry groups) provide power analyses for each category. If there is a plan to test for gene-gene interaction effects, address power for that particular design (e.g., testing gene-gene interactions separately from main effects and/or jointly).

When describing the range of detectable effect sizes, include a brief discussion of the likelihood that there are relevant loci within the detectable range. Be sure to put this discussion in the context of trait heritability and results from previous studies that attempted to localize risk loci. If the plan is to incorporate results from other studies in the analysis to increase study power, explain how this will be accomplished.

Data Analyses: Provide a thorough and detailed plan for data analyses. Examples of the expected elements in this section include the analytical approaches to be used and their justification; plans for quality control analyses of genotypic data; methods to account for genotypic and phenotypic uncertainty, if relevant (e.g., diagnostic uncertainty would be an example of phenotypic uncertainty); plan to control for possible confound of genotype and phenotype due to ancestry; how false positive rates will be controlled in light of multiple testing; whether gene-gene and/or gene-environment interactions will be evaluated; and, if relevant, how the trait or locus will be localized. If imputation will be used to combine the data obtained with earlier data describe the imputation plan.

Provide a clear summary of the team's expertise and experience with the kind of analyses proposed. Be explicit about the role of each team member and who will lead the analysis effort. Explain the approximate amount of dedicated time each member will devote to the effort.

Data Management: Provide a description of the institutional computing resources that will be available to this study. Describe how the data are to be managed, such as type of data base, who will maintain and update it, and who will have access to it. Highlight experience with data management for large data sets, such as those to be produced by the proposed project. Describe strategies for data security.

Plans for the Next Phase: Describe plans for follow up studies: e.g., additional genotyping and/or DNA sequencing, replication studies, or functional testing of variants. If collaborations have been established for follow up, include these letters of collaboration.

If you have questions, please contact: Camilla.day@nih.gov