



ClinGen Gene Curation Expert Panel (GCEP) Quick Guide

The increasing number of claimed associations between diseases and putative disease-causing genes has generated a complex molecular diagnostic testing environment and a critical need for systematic evaluation of the “clinical validity” of these assertions. [ClinGen Gene Curation Expert Panels](#) (GCEP) are multi-institutional teams with broad expertise in a particular field or condition of interest that are approved and follow the ClinGen [clinical validity process](#) to reproducibly classify gene-disease relationships based on the strength of the evidence for an asserted association with a disease of interest (see Figure 1 below).

Step 1: Define your Gene Curation Expert Panel and Plans:

- A. **Identify the group composition:** Broad representation of the community of experts is strongly encouraged to ensure a wide range of opinions are reflected and to mitigate issues with COI.
 - Include at least 3 independent experts from different institutions.
 - Identify roles and responsibilities for GCEP members:
 - i. Content experts for relevant genetic and functional evidence AND at least one member with expertise in the ClinGen clinical validity framework.
 - ii. A ClinGen staff member (biocurator and/or coordinator) or Gene Curation WG (GCWG) member may be embedded.
 - iii. For groups without ClinGen representation, there should be periodic interactions with the GCWG.
- B. **Define scope of work (disease focus and gene list to be curated):** Create a list of genes to be curated and identify any issues with defining the appropriate disease entity (lumping and splitting)
 - Utilize [ClinGen Lumping and Splitting guidelines](#) during pre-curation.
 - Focus on the canonical disease and avoid splitting into multiple individual phenotypes.
 - GCEPs will utilize the ClinGen Gene Tracker, a system that houses each groups gene list and the pre-curation data consistent with the current Lumping and Splitting Guidance.
 - i. Access to the Gene Tracker occurs after GCEP application approval.
- C. **Address conflict of interest (COI):** GCEP members will be asked to disclose COI and other existing or planned independent curation efforts that could potentially overlap with the scope of ClinGen work.
 - Members will be expected to self-manage and declare COI on a survey sent by the coordinator.
 - i. Academic (discoverer of a gene that is relevant to their SOW)
 - ii. Financial (lab director/employee of a commercial laboratory)
 - COI will be declared publicly on the group’s roster on the [clinicalgenome.org](#) website.
 - Authors of literature about relevant genes and commercial entities should not be the arbiter of a classification when there is limited data and it was provided by that individual or entity.
 - i. No special measures are needed if there is group consensus on a gene classification; otherwise, those with relevant COI should refrain from decision-making.
- D. **Submit attestation document:** The GCEP leader(s) will submit the checkbox attestations document to the CDWG Oversight Committee on behalf of the GCEP.

- This GCEP will utilize the ClinGen [Gene Tracker](#) for documentation of all pre-curation information, consistent with the current [Lumping and Splitting working group guidance](#) for gene-disease relationships.
- This group will utilize the ClinGen Gene Curation Interface for documentation of all gene-disease validity classifications.
- All curations completed by this group are expected to be made publicly available through the ClinGen website upon completion.
- The [ClinGen publication policy](#) should be reviewed and a manuscript concept sheet should be submitted to the NHGRI and ClinGen Steering Committee before the group prepares a publication for submission.
- Draft manuscripts must be submitted to the ClinGen Gene Curation WG for review prior to submission (see Resources Table below for email).

Submit completed Step 1 application materials to the ClinGen CDWG Oversight Committee.

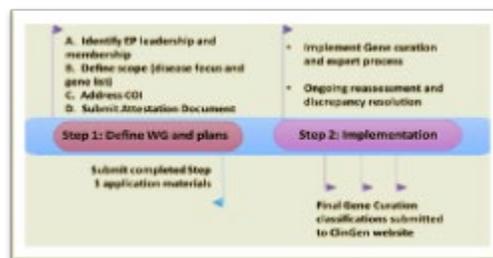


Fig. 1: ClinGen Gene Curation Expert Panel process

Step 2: Implementation

- Develop a curation and review protocol to implement the ClinGen framework¹; for example, successful approaches include:
 - Single biocurator curation with comprehensive GCEP review (presentation of all data on calls with GCEP votes). Note: definitive genes may be expedited with brief summaries.
 - Paired review (biocurator & domain expert) with expedited GCEP review. Expert works closely with a curator on the initial summation of the information for expedited GCEP review (brief summary on a call with GCEP voting and/or electronic voting by GCEP). Definitive genes can move directly from biocurator to expedited GCEP review.
 - Dual biocurator review with expedited GCEP review for concordant genes and full review for discordant genes.
- Biocurators should become familiar with the [gene curation training materials](#) and the [lumping and splitting materials](#) on the clinicalgenome.org website.
- Biocurators should join the Biocurator WG mailing list
 - The Biocurator Working Group conducts calls that occur every 2nd and 4th Thursday from 12-1pm ET.
- Contact geneuration@clinicalgenome.org to schedule a training session on the use of the Gene Curation Interface (GCI).

NHGRI Pre-print Policy

It is the expectation for all ClinGen-supported GCEPs that whenever possible, manuscripts will be pre-published (e.g. medRxiv, bioRxiv, etc). If the authors do not anticipate submitting their manuscript for pre-publication they must provide a written justification in their GCEP application.

Resources:

Expert Panel Application help	cdwg_oversightcommittee@clinicalgenome.org
Gene Curation Working Group	geneuration@clinicalgenome.org
Biocurator Working Group	biocurator@clinicalgenome.org
Gene Curation Interface (GCI) help	clingen-helpdesk@lists.stanford.edu
Gene Tracker Help	clingentrackerhelp@unc.edu

¹Strande, NT et al. (2017). AJHG. 100(6):895-906. PMID. 28552198. [doi: 10.1016/j.ajhg.2017.04.015](https://doi.org/10.1016/j.ajhg.2017.04.015).

Web Resources (summarized from hyperlinks above):

Gene Curation WG: <https://www.clinicalgenome.org/curation-activities/gene-disease-validity>

ClinGen Gene Curation training materials:

<https://clinicalgenome.org/curation-activities/gene-disease-validity/training-materials/>

Lumping and Splitting materials:

<https://clinicalgenome.org/working-groups/lumping-and-splitting/>

ClinGen Publication Policy:

https://www.clinicalgenome.org/site/assets/files/3752/clingen_publication_policy_apr2019.pdf