

## **ClinGen General Sequence Variant Curation Process Standard Operating Procedure**

### **List of updates**

#### **Updates from Version 1.0 to Version V2.0 (January 2021)**

Please note that all updated sections are highlighted in yellow in the “Variant Curation SOP 2.0\_Updates Highlighted” document.

- A list of frequently used terms has been added at the beginning of the document.
- All screenshots throughout the document have been updated to reflect the re-architecture of the VCI, implemented in December 2020.
- New sections have been added on “Getting Started” (Section 2), “General Navigation” (Section 3), “General Organization of the VCI” (Section 4), “Selecting a Variant for Curation” (Section 5), and “Associating a Variant with a Disease and Mode of Inheritance” (Section 6). While these details are also covered in the VCI Help document, this information has now been incorporated into the SOP as well based on feedback from curators.
- A “Summary of steps for criteria evaluation” has been added (Section 8.3)
- Details on transcripts have been updated to reflect the use of MANE-Select transcripts (Section 9.1. under “Transcript information”
- The in silico predictors sections under “Missense sub tab” (Section 9.3) has been re-organized and the splice site predictors section is updated; details on HumanSplicingFinder have been removed because this resource is no longer freely available, and information on SpliceAI and varSEAK have been added. Links to SpliceAI and varSEAK user interfaces are now available in the VCI.
- Experimental studies (Section 9.4) has been updated to include information on the publication on the latest functional studies guidance.
- The entire on the Case/Segregation tab (Section 9.5) has been updated to reflect the reorganization of this tab from Release 28. This includes the ability to record information from PMIDs and other sources, such as clinical laboratories.
- Various other small edits have been made throughout.