Reanalysis of Exome or Genome Sequencing Data

I. Reanalysis of exome or genome sequencing data is considered **medically necessary** when[1]:

   A. The member had exome or genome sequencing at least 18 months ago, **OR**

   B. The member's phenotype has expanded to include clinical findings[2] that were not present at the time of the initial exome or genome sequencing analysis, **AND**

      1. Results of prior exome or genome sequencing do not explain these new clinical findings.

II. Reanalysis of exome or genome sequencing data is considered **investigational** for all other indications.

[1]If reanalysis of exome data is not possible, see the genome sequencing criteria for additional coverage information.

[2]See Standard Exome Sequencing or Standard Genome Sequencing criteria for qualifying clinical findings.

DEFINITIONS

1. **Exome Sequencing** (ES) is a genomic technique for sequencing all of the protein-coding regions of genes in the genome (also known as the exome).
2. **Exome sequencing reanalysis** or **Reanalysis of exome** may not be possible in some situations. Sequencing platforms may have changed substantially enough that the performing lab can no longer use the data from the original ES in their pipeline. Specifically, ES reanalysis may not be possible if there have been improvements in technology/chemistry (e.g., new methods for DNA capture and/or sequencing), bioinformatics advancements, or there is new information regarding

the genetic etiology of a condition that could explain the patient's clinical features and would not have been able to be detected by the previous exome sequencing.

3. **Genome Sequencing** (GS) is a genomic technique for sequencing the complete DNA sequence, which includes protein coding as well as non-coding DNA elements.

REFERENCES

1. Deignan JL, Chung WK, Kearney HM, et al. Points to consider in the reevaluation and reanalysis of genomic test results: a statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2019;21(6):1267-1270. doi:10.1038/s41436-019-0478-1
2. Alfares A, Aloraini T, Subaie LA, et al. Whole-genome sequencing offers additional but limited clinical utility compared with reanalysis of whole-exome sequencing. *Genet Med*. 2018;20(11):1328-1333. doi:10.1038/gim.2018.41
3. Tan NB, Stapleton R, Stark Z, et al. Evaluating systematic reanalysis of clinical genomic data in rare disease from single center experience and literature review. *Mol Genet Genomic Med*. 2020;8(11):e1508. doi:10.1002/mgg3.1508
4. "Genomic Sequencing for Rare Disease". Seattle Children's Hospital Patient-centered Laboratory Utilization Guidance Services. https://www.schplugs.org/wp-content/uploads/Genomic-Sequencing-in-Rare-Disease_2023_FINAL.pdf. July 2023
5. Reddi HV, Avenarius MR, Bean LJH, et al. Addendum: Points to consider in the reevaluation and reanalysis of genomic test results: A statement of the American College of Medical Genetics and Genomics (ACMG). Genetics in Medicine. 2024;26(5):101100. doi:10.1016/j.gim.2024.101100