The aim of this external quality assessment (EQA) was to provide an online competency assessment for laboratories routinely performing interpretation and classification of CNV and SNV variants.

Participants were required to classify 10 copy number variants (CNVs) and 5 single nucleotide variants (SNVs) and state whether the variants were consistent with the clinical phenotype.

Variants were delivered using an online tool for CNVs and SNVs. This EQA has been developed for genocentric centres to demonstrate the competency of laboratories performing variant classification and to identify any unmet training needs.

AIM OF EXTERNAL QUALITY ASSESSMENT EXERCISE

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VARIANT CLASSIFICATIONS

➢ Aim is to assess a laboratory's competency to determine the pathogenicity (and classification) of CNVs and SNVs.

➢ All clinical case scenarios were based on real patients.

➢ Presented with 12 postnatal cases each with one CNV variant for classification.

➢ Present with 3 cases with clinical indication of a monogenic disorder with either one or two SNV variants for classification.

➢ Laboratories were provided CNVs or SNVs ranging from class 1 (benign) to class 5 (pathogenic).

➢ Participants were required to apply their usual processes to classify each variant.

➢ Participants were required to check the referral information with either the array (CNV) or Next Generation Sequencing (SNV) results.

➢ More than 200 laboratories participated from 34 countries.

RESULTS OF CLASSIFICATION OF THE VARIANTS

Bubble plots of expected classification versus other classifications for each variant.

The size of the bubble indicates the proportion of individuals that provided a specific classification. The mean bubble represents the expected classification.

SUMMARY

➢ There was global participation in both the CNV and SNV EQAs. The submissions were scored, reported to each laboratory and the Summary EQA Report provided the expected classification together with evidence for the classification and an overview of the findings.

➢ In some case scenarios where the laboratory classification was incorrect, this would have affected patient management adversely.

➢ These EQAs provide competency assessment for laboratories routinely performing variant classification and also identifies any unmet laboratory training needs. We demonstrate the challenges associated with variant classification and highlight the need for education, competency assessment and standardisation worldwide.

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