Synopsis of Approach to Genetic Diagnosis in Developmental Delay

- Primary care providers may consider initiating genetic diagnostic testing for patients with developmental delay when access to genetic services is limited.
- The American Academy of Pediatrics has published their statement on appropriate genetic evaluation of children with developmental delay: see Moeschler et al Pediatrics 2014.
- Ensure that acute neurological concerns are addressed with appropriate evaluation and not deferred until after genetic testing.
- Referrals for developmental therapies should be made concurrently with a genetic evaluation.

- Our recommendations are as follows:
  - Tier 1
    - Chromosomal microarray
    - Fragile X trinucleotide repeat analysis
  - Tier 2
    - Large gene sequencing panel of developmental delay-associated genes
  - Tier 3
    - Whole exome or whole genome sequencing may be considered.
    - See www.treatable-id.org for a testing algorithm and information on diagnoses that have specific treatment and can be diagnosed with biochemical testing.
      - Serum amino acids
      - Serum homocysteine
      - Urine creatine metabolites
      - Urine organic acids
      - Urine purines and pyrimidines
      - Urine oligosaccharides
      - Urine mucopolysaccharides

- Families should undergo appropriate informed consent specific to the test that is planned before sending genetic testing (see attached document).
- Ensure that insurance approval is obtained prior to testing to avoid large out-of-pocket expenses; this may be performed by the provider's office or as a benefits investigation by the lab performing the testing (if that service is offered by the lab; see attached document).
- Most genetic tests can be performed on a buccal swab rather than a blood sample.
- Labs will classify each reported genetic variant as either benign, likely benign, variant of uncertain significance (VUS), likely pathogenic or pathogenic.
- Likely pathogenic or pathogenic results can usually be reported as diagnostic to families if clinical features are compatible with that diagnosis.
- A VUS may require interpretation from a geneticist to determine clinical significance and may require follow up testing of the child and other family members.

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MSRGN would like to thank all the professionals, individuals and families who assisted in the review of the documents.

Acknowledgement
This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $600,000 with 0 percentage financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.