



Division of Human Genetics

## Shwachman-Diamond syndrome (SDS) Genes Tested: *SBDS*

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Additional information and test requisitions are available at:  
[www.cincinnatichildrens.org/molecular-genetics](http://www.cincinnatichildrens.org/molecular-genetics)



*Helping you fit the  
pieces together*

### Shipping Instructions

Please enclose test requisition with sample. All information must be completed before sample can be processed.

Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:  
Cytogenetics and Molecular Genetics  
Laboratories  
3333 Burnet Avenue NRB 1042  
Cincinnati, OH 45229  
513-636-4474

**Shwachman Diamond syndrome** is a severe genetic disorder characterized by exocrine pancreatic dysfunction, hematologic abnormalities including neutropenia or multi-lineage cytopenia and predisposition towards myelodysplastic syndrome (MDS) or acute myelogenous leukemia (AML) and bone abnormalities. It is the second most common cause of congenital exocrine pancreatic insufficiency after cystic fibrosis. The incidence of SDS is approximately 1 in 76,000 births and occurs in all populations. Neonates with SDS are typically asymptomatic. Children with SDS typically present within the first year of life with failure to thrive and poor growth due to pancreatic insufficiency in addition to recurrent infections secondary to neutropenia. Malignant transformation, i.e. myelodysplasia and acute myelogenous leukemia, is a significant risk in individuals with SDS. Treatment with granulocyte colony-stimulating factor (G-CSF) reduces the duration and severity of the neutropenia and improves clinical outcome. Hematopoietic stem cell transplantation may be indicated for severe disease.

The diagnostic criteria for SDS include:

- Pancreatic dysfunction
- Neutropenia

However, many patients present in an atypical fashion. An expanded set of diagnostic criteria and further information about SDS can be found on the North American SDS Registry website at [www.sdsregistry.org](http://www.sdsregistry.org).

Shwachman Diamond syndrome is inherited as autosomal recessive condition. Biallelic mutations in the Shwachman Diamond gene, ***SBDS***, which maps to 7q11, are found in approximately 80% of individuals who meet the diagnostic criteria for SDS. *SBDS* consists of five exons and encodes a 250 amino acid protein which plays a role in RNA metabolism, ribosome biogenesis and protein translation. Mutations involving all five exons have been described. Three common mutations account for 76% of the SDS-causing alleles. Two of these common mutations may occur on the same allele (in cis) which results from gene conversion due to recombination with the *SBDS* pseudogene (*SBDSP*). Therefore, parental analyses may be required to determine the clinical significance of these mutations in the proband and in at-risk siblings. No genotype-phenotype correlations have been reported with specific *SBDS* mutations and considerable phenotypic variability is observed, even among siblings.

### INDICATIONS:

- Confirmation of diagnosis in a symptomatic individual
- Carrier/Heterozygote detection in individuals with a family history of SDS.
- Prenatal diagnosis of an at-risk fetus, after confirmation of mutations in the parents (by prior arrangement only)
- Presymptomatic diagnosis in an at-risk sibling or potential HSCT donor

## SPECIMEN:

At least 3 mL whole blood in lavender top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. **Buccal samples are required for analysis in patients who have undergone bone marrow transplantation and may facilitate DNA isolation in patients undergoing chemotherapy or in individuals with leukopenia.** Please call for a free buccal (cytobrush) collection kit.

## METHODOLOGY:

Testing is performed by PCR-based sequencing of the entire coding regions and intron/exon boundaries of the *SBDS* gene.

## SENSITIVITY:

The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions, and insertions in the regions analyzed. Large deletions involving single or multiple exons, large insertions, genetic recombinational events and rare, primer site mutations may not be identified using these methods. Parental studies are sometimes necessary to determine the phase of identified sequence variants.

## TURN-AROUND TIME:

30 days

When needed for interpretation, parental analyses may extend the turn around time.

## COST:

**Please call 1-866-450-4198 for institutional pricing or for any billing inquiries**

## CPT CODES:

<i>SBDS</i> full gene sequence analysis	81479
Family specific mutation analysis	81403

## RESULTS:

Results will be reported to the referring physician or health care provider as specified on the requisition form.