



## Service Description

### Duchenne & Becker Muscular Dystrophy (DMD & BMD)

#### 1 Background

Duchenne Muscular Dystrophy (DMD) OMIM#310200

Becker Muscular Dystrophy (BMD) OMIM#300376

DMD is an X-linked recessive disorder, and is the most common form of muscular dystrophy, occurring in about 1 in 3,500 males. BMD is a milder allelic form, with a lower prevalence of 1 in 18,500 live male births. Typical clinical indications include elevated Creatine Kinase (CK) levels, calf pseudohypertrophy, absence or reduction of Dystrophin protein in immunohistochemistry of muscle biopsy, and Gower's sign (a characteristic manner of rising from a sitting to standing position).

DMD and BMD result from mutations in the *DMD* gene, which encodes the protein Dystrophin. Approximately 65% of DMD and 85% of BMD males have a deletion within the *DMD* gene. Duplications are found in around 5-10% of affected patients.

#### 2 Standard service

##### A Essential referral information

In addition to supplying standard patient identification and referral information (see Section I below), the following should be clearly indicated:

1. Patient's symptoms
2. Any family history, including names, dates of birth, relationship, details of any clinical diagnoses, and genetic test results if available.

Please note: It is the responsibility of the referring clinician to ensure consent has been obtained for testing and storage.

##### B Samples required

- Generally 5-10ml of EDTA blood (FBC bottle) is required. Sample identification policy is detailed at (see Section I below).
- Blood specimens must be appropriately packaged (see Section I), and preferably sent by courier to arrive as soon as possible. Do not freeze prior or during postage.
- Please note that extracted DNA is stored from patient's samples at the National Centre for Medical Genetics, and kept indefinitely unless a written request for its disposal is received from the patient or their parent/guardian.

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Dublin, Ireland  
**Division of Molecular Genetics**

**C Restrictions on testing**

- Carrier testing is not offered for minors. This policy is consistent with international guidelines for genetic testing of children.
- Carrier testing is only performed following a referral to, and consultation with, a clinical genetics service. This is in line with international guidelines on genetic testing. Please contact the Clinical Genetics Division of NCMG regarding referrals <link to [Clinical contacts homepage](#)>.
- Prenatal testing must be arranged in advance with the laboratory, through a Clinical Genetics department if possible.

**D Tests offered**

*Diagnostic testing:*

Molecular confirmation of a suggested clinical diagnosis is possible, using a multiplex ligation-dependent probe amplification (MLPA) assay which tests for copy number changes in each exon of the *DMD* gene.

*Carrier testing:*

Carrier testing may be possible for females with a family history of DMD/BMD.

- 1) In general, the index case must have a diagnosis of DMD/BMD, which has been confirmed by identification of the causative mutation. Carrier testing is then based on direct analysis of the *DMD* gene.
- 2) Carrier testing (using linked markers) may also be possible in cases where a causative mutation has not been identified, as long as a firm diagnosis can be established by other means. Please contact the laboratory in advance to discuss the possibility of testing for such families.

*Prenatal testing:*

Prenatal testing must be arranged in advance with the laboratory, through a Clinical Genetics department if possible. As fetal sexing from a maternal blood specimen is possible, this test is generally requested to establish gender prior to an invasive prenatal DMD/BMD test being requested. Regarding prenatal testing specifically for DMD/BMD:

- 1) In general, the index case must have a diagnosis of DMD/BMD, which has been confirmed by identification of the causative mutation. Prenatal testing is then based on direct analysis of the *DMD* gene.
- 2) It may be possible to also offer prenatal diagnosis (using linked markers) in families where a causative mutation has not been identified, as long as a firm diagnosis can be established by other means. Please contact the laboratory in advance to discuss the possibility of testing for such families.

**E Diagnostic Sensitivity of tests**

Like most molecular genetic tests, the diagnostic sensitivity of the DMD/BMD tests is less than 100%.

*Diagnostic testing:*

The MLPA assay detects all whole exon deletions and duplications, but approximately 5% to 10% of boys with BMD, and 25% to 30% of boys with DMD, do not have whole exon deletions or duplications, but have other small insertions/deletions/point mutations etc. which are not detected by this test.

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**Carrier testing:**

- 1) Where the causative mutation is known, carrier status can be determined at an accuracy of >99%.
- 2) If the mutation has not been identified in the index, it may be possible to use linkage analysis to modify the estimated risk of carrier status. However, the diagnostic sensitivity of such analysis is dependent on factors which are unique to each family assessed.

**Prenatal testing:**

- 1) Where the causative mutation is known, a diagnostic prediction can be made at an accuracy of >99%.
- 2) If the mutation has not been identified, and prenatal diagnosis by linkage analysis is appropriate, the diagnostic sensitivity is dependent on factors which are unique to each family assessed.

**F Interpretation:**

Results are given in the form of a written interpretative report to the referring clinician. For example, for diagnostic tests a diagnosis is confirmed where a deletion or duplication within the DMD gene is detected. The absence of a deletion and/or duplication does not exclude a diagnosis of DMD/BMD, since a proportion of cases result from other types of mutation.

**G Target reporting times:**

As reporting times are constantly evolving, please refer to [www.genetics.ie/molecular](http://www.genetics.ie/molecular), or contact the molecular genetics laboratory, to receive up-to-date information on anticipated reporting times for your referral.

- The following are current target reporting times for each category of test offered (information correct as of 17/12/2009):
  - Routine Query Affected- 6 weeks
  - Urgent Query Affected (i.e. a neonate)- 2 weeks
  - Routine Carrier Status- 6 weeks
  - Urgent Carrier Status (eg. pregnancy) - 2 weeks
  - Prenatal Diagnosis (CVS)- 2 weeks
  - Prenatal Diagnosis (Amniotic fluid sample)- 4 weeks
- Please contact the laboratory if you have not received a report within a week of your patient being due back in clinic.
- Please note it is our policy not to issue verbal results.
- Request for copies of reports on the day that your patient is in clinic cannot normally be accommodated. We usually require 24 hours notice in which to fax a copy of a report.

**H Further tests**

**Diagnostic testing:** Where MLPA does not identify a causative mutation, for a patient in whom a clinical diagnosis of DMD/BMD is considered likely, it is possible to screen for other types of mutations. This service is available through an external laboratory, using a method predicted to detect greater than 98% of all DMD/BMD mutations, and at a cost of up to stg£700. Please contact us to make arrangements for such testing, if required.

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**I Web Links to Related Documents**

Standard referral information/NCMG request form

[http://www.genetics.ie/pir/2006\\_NCMG\\_Referral\\_Form.pdf](http://www.genetics.ie/pir/2006_NCMG_Referral_Form.pdf)

Sample/Patient identification policy

<http://www.genetics.ie/pir/SampleIdentificationPolicyWeb.pdf>

Packaging of specimens for transport

[http://www.genetics.ie/pir/sending\\_samples.pdf](http://www.genetics.ie/pir/sending_samples.pdf)

Please note that hard copies of the above documents may be requested from:

*Division of Molecular Genetics, National Centre for Medical Genetics, Our Lady's Children's Hospital, Crumlin, Dublin 12. Tel: 01 4096733; Fax: 01 4096971*

*The NCMG Molecular Genetics laboratory participates in external QA schemes run by the UK NEQAS for Molecular Genetics, the European Molecular Genetics Quality Network (EMQN), and the Cystic Fibrosis European Network. Results of assessments are available for inspection upon request.*

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