

## ***Frequently Asked Question: What tissue types will MGL accept for DNA extraction?***

### **Summary:**

The following tissue types are routinely accepted for DNA extraction in MGL:

- Blood (EDTA)
- Bone marrow (for chimerism studies only)

The following tissue types can generally be submitted ***following consultation with MGL:***

- DNA previously extracted in another ***clinical*** molecular genetics laboratory
- Chorionic villus sample (CVS) / placental biopsy / cultured villi
- Cultured amniocytes / direct amniotic fluid
- Frozen tissue specimens obtained during post-mortem examination (e.g., muscle, liver, spleen)
- Other tissue culture (e.g., skin fibroblasts; requires consultation with a lab that will culture the tissue sample)

Due to issues related to the validation of our test methods, the availability of reagents for DNA extraction and the amount and/or quality of DNA obtained from other tissues, MGL **cannot** generally accept other tissue types (e.g., buccal swabs, saliva, blood spot cards or formalin-fixed tissue specimens) for DNA extraction and testing. Contact MGL to discuss specific cases where collection of blood for DNA extraction is not possible.

### **Detailed discussion:**

MGL is aware that some patients and/or their families may be reluctant to undergo venipuncture to allow for blood collection for the purpose of DNA extraction and genetic testing. However, there are both practical and technical reasons why MGL is not currently able to accept other tissue types.

MGL currently receives approximately 9000 specimens per year for DNA extraction and testing. The vast majority of the specimens submitted are blood samples, and DNA is extracted commercial DNA extraction kits and automated systems specifically for blood samples. When an alternate tissue type is submitted, DNA extraction is performed manually.

All of the tests performed in MGL are validated using DNA extracted by specific methods. Validation of clinical tests is not only a formal requirement for laboratory accreditation, it is essential to ensure the safety, accuracy and utility of a specific clinical test. Because certain molecular genetic tests can be affected by DNA extraction method and/or tissue source, validation studies must be undertaken when a new DNA extraction method or tissue source is introduced for use in MGL. In addition, DNA extraction from alternate tissue samples requires the purchase of additional DNA extraction kits. MGL does not receive enough samples to justify validating all of our assays for the use of DNA from other tissue sources or to purchase of DNA extraction kits for use with alternative tissue types.

Other issues specific to each alternate tissue type are reviewed below.

### ***DNA extracted in other clinical laboratories***

For most assays performed in MGL, DNA extracted in other clinical molecular laboratories can be accepted. Certain assays are sensitive to extraction method, however, so we recommend consulting with MGL prior to requesting transfer of DNA. DNA extracted in research laboratories is **not** accepted in MGL for clinical testing.

### ***Prenatal specimens***

MGL will generally accept prenatal specimens (CVS, amniocentesis and the like). However, we require advanced notice to ensure that prenatal diagnosis is available for the test requested and, as the validity of some tests depends on the time during pregnancy at which the sample is collected, that the most appropriate sample type is obtained.

### ***Saliva and buccal swabs***

The DNA in saliva or buccal swab samples comes from many sources, including blood, buccal cells and non-human DNA from bacteria and food particles. DNA obtained from these tissues is also often contaminated by proteins or other organic substances. Contamination is the most significant limiting factor in the use of these tissue types as sources of DNA in MGL.

As an example of the negative impact these contaminants have on our assays, attempts to use DNA from saliva for fragile X testing by Southern blot have been unsuccessful due to inhibition of the restriction enzyme digestion required for the distinction of normal and abnormal banding patterns. This can lead to false positive results making DNA from saliva unsuitable for this assay. This also provides a useful example of why sample-specific validation of each assay is required.

In addition to providing DNA with a higher degree of contamination, saliva and buccal samples provide significantly less DNA than extraction from blood; insufficient DNA may be obtained to perform specific tests.

Commercial collection kits are available that may improve the quantity and quality of DNA extracted from these tissues. However, MGL is not funded to provide kits for the purposes of sample collection. Further, even in the event that a clinician or patient provides the collection kit themselves, MGL generally does not have the DNA extraction kits required for the extraction of DNA from these sources.

In addition to the technical issues of extracting sufficient high-quality DNA from these tissue types, saliva and buccal swab collection kits are often used by patients and families to collect their own samples, which increases the risk of sample mix-up and contamination.

### ***Blood spot cards***

The amount of DNA that can be obtained is significantly less than what can be obtained from blood. DNA quality may also be adversely affected if the blood spot cards have been stored for an extended period of time.

As with saliva and buccal swab collection kits, since blood spot cards are often used by patients and families to collect their own samples, the risk of sample mix-up and contamination is increased with these samples.

***Formalin-fixed, paraffin-embedded tissue***

Fixing an organic specimen in formalin and embedding it in paraffin is a very common technique used to preserve clinical specimens. However, the use of formalin as a preservative causes extensive modification of nucleic acids that impacts the utility of these specimens for most genetic testing. Although DNA can be extracted from these tissues, the DNA obtained is generally highly fragmented and is therefore unsuitable for MGL's tests, which currently require a higher molecular weight DNA than that obtained from this tissue source. In general, the greater the amount of time a tissue sample is kept in formalin prior to being embedded in paraffin, the less likely the tissue will yield a DNA sample suitable for use in MGL.