WHY UPDATE THE NF1 DIAGNOSTIC CRITERIA?

While research has uncovered many new discoveries in NF1, there have not been any updates to the way patients are diagnosed with NF1 since 1987. The original official diagnostic criteria were established prior to:

• Discovery of the gene that causes NF1
• Ability to perform genetic testing
• New clinical information about NF1
• Newly described conditions that have similar manifestations as NF1

An international group of NF experts reviewed and updated the NF1 diagnostic criteria to include the latest in NF research and clinical findings. This will help improve patient diagnosis and care.

A glossary of terms can be found on the second page.

THE NF1 DIAGNOSTIC CRITERIA

ORIGINAL DIAGNOSTIC CRITERIA (1988)

A diagnosis of NF1 can be given if an individual has two or more of the following manifestations:

• Six or more café-au-lait macules (brown skin spots)
  » greater than 5mm in pre-pubertal children
  » greater than 15mm in post-pubertal individuals
• Freckling in axilla (armpit) or groin
• Two or more neurofibroma tumors of any type, or one plexiform neurofibroma
• Two or more iris Lisch nodules (iris hamartomas)
• Optic glioma

• A distinctive bony lesion: dysplasia (abnormal growth) of the sphenoid bone behind the eye, or dysplasia of long bones, often in the lower leg
• Having a close relative (parent, sibling, or child) with NF1

UPDATED DIAGNOSTIC CRITERIA (2021)

A diagnosis of NF1 can be given if an individual has two or more of the following manifestations:

• Six or more café-au-lait-macules* (brown skin spots)
  » greater than 5mm in pre-pubertal children
  » greater than 15mm in post-pubertal individuals
• Freckling in axilla (armpit) or groin*
• Two or more neurofibroma tumors of any type, or one plexiform neurofibroma
• Two or more Lisch nodules or two or more choroidal abnormalities
• Optic pathway glioma (tumor of the visual pathway)
• A distinctive osseous lesion such as: sphenoid dysplasia; anterolateral bowing of tibia (tibial dysplasia); or pseudarthrosis of a long bone
• A pathogenic NF1 gene variant **
• A parent with NF1 by the above criteria

*At least one of the two pigmentary findings (café-au-lait macules or freckling) should be bilateral.
**GLOSSARY**

- **Anterolateral bowing of tibia** is a curving of a bone in the leg
- **Café-au-lait macules**, also called café-au-lait spots, are flat darkened areas on the skin
- **Choroidal abnormalities** are problems with the vascular layer of the eye (the choroid)
- **Dysplasia** means abnormal growth
- **Lisch nodules** are small tan or brown bumps on the surface of the iris in the eye
- **Neurofibroma** is a tumor that forms on a nerve cell sheath
- **Osseous lesion** is a problem with a bone that is not due to injury
- **Optic pathway glioma** is a tumor of the visual pathway
- **Pathogenic variant** is a change in a gene that causes a problem, formerly called a mutation
- **Pseudarthrosis** is a condition that occurs when the bones in the leg do not heal correctly
- **Sphenoid** is a bone near the base of the cranium behind the eye

**Additional Genetic Criteria Updates:**

- The term “mutation” is no longer accepted in genetics; **pathogenic variant** is now the preferred term.
- Genetic analysis is not REQUIRED for diagnosis but may allow for an earlier diagnosis.
- Genetic analysis ALONE is not sufficient to diagnose NF1 - diagnosis also requires a second diagnostic feature of NF1.