# HEALTH CARE PROVIDER FACT SHEET

## Phenylketonuria (PKU) Prenatal/Pre-conception Testing of the Phenylalanine Hydroxylase (PAH) Gene

It has come to the attention of some metabolic centers that some families have been counseled incorrectly about PAH deficiency. We are hoping this information will help you to provide accurate information to families where parents are carriers of variants in the PAH (Phenylalanine Hydroxylase) gene.

The PAH gene is responsible for the disorder ***Phenylketonuria (PKU)***, and the PAH gene also can also cause milder conditions than classical PKU, including ***mild PKU*** and ***benign hyperphenylalaninemia*** (***HPA or hyperphe***). ***Hyperphe*** means there is higher than the typical amount of phenylalanine in the blood. Some people with elevated Phe need treatment with a special diet or medication whereas other do not require treatment.

***Benign hyperphe*** is a mild form of PAH deficiency, which is typically not associated with clinical symptoms. Classification of PAH deficiency varies, but generally benign hyperphe is when blood Phe remains in the 120-360 µmol/L range and does not require treatment, whereas hyperphe in the 360-600 µmol/l range is generally treated with sapropterin or mild dietary changes. Hyperphe of <360 µmol/L will require infrequent visit for monitoring, whereas hyperphe 360-600 µmol/l on treatment will require regular monitoring and visits (on average once to twice a year after the first year). Females with hyperphe who are pregnant (known as maternal HPA) will have blood phenylalanine monitoring before and during a pregnancy because of the risk of damage to the fetus. Treatment, even mild treatment, might be required during pregnancy for a woman with hyperphe.

***PKU*** has been identified through newborn screening and successfully treated for 60 years. People with classical PKU on adequate treatment have normal growth and development, and have IQ scores within the normal range. People with PKU (even with treatment) are at risk for issues involving language skills, memory, learning skills, and executive function. In the experience of our center, our young adult patients who have had well-controlled PKU during childhood are mostly indistinguishable from their peers in terms of cognitive abilities, higher education, occupations and relationships. Females with PKU who are pregnant (known as maternal PKU) will have blood phenylalanine monitoring and treatment before and during a pregnancy because of the risk of damage to the fetus.

In counseling families about PAH deficiency, we recommend searching for your patients' genetic variants on the ***BioPKU database*** to accurately predict if they are at risk for PKU or hyperphe using the following web tool: http://www.biopku.org/biopku/search-start.asp

Consider consultation with a metabolic center to further discuss genotype and expected phenotype. For more information about PAH deficiency and PKU, please see:
https://www.ncbi.nlm.nih.gov/books/NBK1504/

https://www.newenglandconsortium.org/pku-open-page.