

## Warmblood Fragile Foal Syndrome Type 1

Warmblood Fragile Foal Syndrome Type 1 (WFFS) is a fatal genetic defect of connective tissue characterized by hyperextensible, abnormally thin and fragile skin that cause extensive lesions of skin and mucous membrane (tissue that lines cavities and covers organs) throughout the body. Other signs of the disease include hyperextension of limb articulations, floppy ears, hydrops (accumulation of fluid in fetus), subcutaneous emphysema, hematomas and premature birth. Signs of the disease are present from birth. Newborn foals have to be euthanized because of poor prognosis for an untreatable condition.

WFFS is caused by a mutation (c.2032G > A) in the *PLOD1* gene (*procollagen-lysine, 2-oxoglutarate 5-dioxygenase1*) that codes for an enzyme important for biosynthesis of collagen, which are complex molecules that provide strength and support to many body tissues. The mutation impairs normal function of the enzyme, which leads to development of the disease. In humans, mutations in this gene are associated with a similar defect known as Ehlers-Danlos Syndrome Type VI.

WFFS is inherited as an autosomal recessive defect, which means that both males and females are equally affected and that two copies of the mutation (WFFS/WFFS) are needed to cause the disorder. Horses that carry one copy (N/WFFS) of this recessive mutation are normal but can transmit the mutation to 50% of their offspring.

The Veterinary Genetics Laboratory offers a DNA test for WFFS. The test benefits clinicians to help with diagnosis of WFFS. The test benefits breeders and owners to identify carriers of WFFS and to select mating pairs accordingly to avoid producing affected foals. Mating between two carriers has a 25% chance of producing affected foals.

**Testing recommendation:** The WFFS mutation occurs in Warmblood horse populations that include Hanoverian, Selle Français, KWPN (Dutch), Oldenburg and Westphalian lineages. In addition, Holsteiner, Wurtemberger, Rhinelander, Gelderlander, Zweibrucker and Bavarian Warmblood breeds are at risk for carrying this disorder. The incidence of carriers in Warmblood horses is estimated to be around 9-11%.

Note: Because of European patent restriction, the VGL accepts orders for WFFS testing from any country, except those located in Europe.

Results are reported as:

N/N	No copies of the WFFS mutation; animal is normal.
N/WFFS	1 copy of the WFFS mutation; animal is normal but is a carrier. Horse can pass on the mutation to 50% of offspring.
WFFS/WFFS	2 copies of the WFFS mutation; horse is affected.

### References:

Winand N. Identification of the causative mutation for inherited connective tissue disorders in equines. United States Department Of Commerce Application Number: 61/486,464; (Filing Date: May 16th, 2011).

Monthoux C, S Brot, M Jackson, U Bleul, J Walter. (2015). Skin malformations in a neonatal foal tested homozygous positive for Warmblood Fragile Foal Syndrome. *BMC Veterinary Research* 11:12. DOI 10.1186/s12917-015-0318-8.