cryobio

Additional Agreement to Use Donor PC 1123

We, _____ (Recipient), and _____ (Partner, if applicable), specifically request and accept frozen semen from Cryobio donor PC 1123. We understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor PC 1123. We have received genetic test results on this sperm donor, and we understand that donor PC 1123 has been found to be a carrier of the following recessive genetic conditions:

Alstrom Syndrome

Biotinidase Deficiency

Alstrom Syndrome (ALMS1 gene): Alstrom Syndrome is a pan-ethnic, autosomal recessive disorder caused by pathogenic variants in the gene ALMS1. Symptoms often develop gradually in infancy, can be variable. Clinical features include short stature and obesity, progressive vision and hearing loss, and chronic inflammation of the liver and kidney, leading to more severe disease. Patients also have spinal abnormalities and endocrine disorders, including insulin-resistant diabetes, hypothyroidism, growth hormone deficiency and sex hormone disorders. While some developmental delay is present, individuals are not expected to be intellectually disabled. Organ dysfunction may result in early death, and most patients do not live past the age of 50. It is not currently possible to predict the severity of the disease based on the genotype. There is no current specific treatment for Alstrom Syndrome, and individuals should be managed based on their specific present symptoms.

Biotinidase Deficiency (BTD gene): Biotinidase deficiency is an autosomal recessive disorder caused by pathogenic variants in the gene BTD. This pan-ethnic disorder affects individuals within the first few months of life. Severe forms of the disorder cause children to experience neurological abnormalities such as seizures, hypotonia, developmental delay, and vision problems as well as hearing problems, respiratory problems, and cutaneous abnormalities. A daily dose of biotinidase can be used as an effective treatment of the disease. However, symptoms such as vision problems, hearing loss, and developmental delay are irreversible if they occur. Several specific variants have been associated with full or partial biotinidase deficiency, and therefore the severity of the disease may be predicted based on the genotype.

Carrier status frequency:
Carrier status frequency is the chance of an individual being a carrier for a genetic condition based on their ethnicity alone prior to any genetic screening. If an individual tests negative as a carrier for a condition or conditions, then the chance of being a carrier is significantly decreased. This remaining risk is known as residual risk, meaning what is the risk of being a carrier even after negative genetic testing. Residual risk data is available directly through sema4's website, sema4.com, or can be requested from Cryobio.

Alstrom Syndrome (ALMS1 gene) carrier status frequency in different ethnicities, from Sema4's website:

Worldwide	1 in 198
African	1 in 202
East Asian	1 in 107
Finnish	1 in 626
European (Non-Finnish)	1 in 168
Native American	1 in 352

South Asian	1 in 256

Biotinidase deficiency (BTD gene) carrier status frequency in different ethnicities, from Sema4's website:

Worldwide	1 in 13
African	1 in 52
Ashkenazi Jewish	1 in 15
East Asian	1 in 324
Finnish	1 in 9
European (Non-Finnish)	1 in 12
Native American	1 in 24
South Asian	1 in 7

Recommendation: Both Sema4 and Cryobio recommend that the recipient, or egg source if different than recipient, be tested for Alstrom syndrome and biotinidase deficiency carrier status and consider genetic counseling. Please refer to Sema4's website, sema4.com, for more information and contact Cryobio with any questions or to arrange genetic counseling. Because the donor was tested by Sema4, Cryobio recommends that the recipient or egg source should be tested by Sema4 as well. We also strongly recommend that you discuss the donor's genetic carrier status results with your health care provider. Finally, we recommend that any future child be notified of this donor's carrier status once they are of reproductive age, as even if they do not have a recessive disease, they could be a carrier and their carrier status could be important to identify risks related to their own reproductive future.

Cryobio has advised us of the following:	Please initial to show your understanding and agreement:
The donor we have chosen has had positive results from genetic testing. These results indicate that the donor is a carrier for Alstrom syndrome and biotinidase deficiency.	Initials: _____ Initials: _____
These genetic conditions are inherited as recessive traits. This means that if both the egg source and the sperm source are carriers for the same condition, there is a significantly higher chance of the resulting child having that genetic condition.	Initials: _____ Initials: _____
By the donor testing positive for carrier status for Alstrom syndrome and biotinidase deficiency, the risk to a resulting child would now be higher than that of the general population.	Initials: _____ Initials: _____
Both the risk of being a carrier and the sensitivity of the genetic testing can vary depending on the individual's ethnicity. When an individual tests negative for carrier status, it does not completely eliminate their chance of being a carrier for that disease. Instead, their remaining (residual) risk of being a carrier is determined by their ethnic background. While a negative result decreases the likelihood that an individual is a carrier, how much that risk is reduced by can vary significantly. For more detailed information regarding the sensitivity of testing and remaining risk after negative screening, please see Sema4's website.	Initials: _____ Initials: _____

Genetic testing looking at a large panel of genes, including the genes/conditions that the donor has tested positive for, is available and could be done.	Initials: _____ Initials: _____
Genetic testing is *strongly recommended* for me (or the egg source, if different) to see if I am a carrier for Alstrom syndrome and biotinidase deficiency.	Initials: _____ Initials: _____
A negative genetic test result in the egg source significantly reduces the likelihood that the resulting child could be affected with these conditions. However, we fully understand that the risk cannot be completely eliminated.	Initials: _____ Initials: _____
While genetic testing can lower the likelihood for certain genetic diseases, no amount of genetic testing can guarantee that a child will be healthy or free of genetic disease.	Initials: _____ Initials: _____
Genetic counseling is available to us, either through Cryobio or Sema4, if we have additional questions regarding these test results and potential risks.	Initials: _____ Initials: _____
Both the donor's carrier status and whether the donor is acceptable for my use should be discussed with my health care provider.	Initials: _____ Initials: _____

We have read the above material and assume the risk of using donor sperm from a donor who has been found to be a carrier of genetic disorders. We are making the choice to use donor sperm from donor PC 1123 willingly and agree to release any legal claims, including negligence, that may arise from or are related to insemination or assisted reproduction using donor sperm from donor PC 1123.

We have read and had the chance to ask questions, and we understand and agree to the terms of this Additional Agreement to use donor PC 1123.

_____
Recipient

_____
Date

_____
Partner, if applicable

_____
Date

William C. Baird, PhD
_____
Cryobio

03-01-2021
_____
Date