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A Guide to an Egg Donor's Genetic Testing Summary (GTS)

What is a GTS?

A GTS is a document that summarizes the results of the genetic testing performed on an egg donor. Its purpose is to provide means by which a suitability match with a sperm source can be performed.

This testing is performed as part of the donor's screening process per the recommendations of the American Society of Reproductive Medicine (Fertil Steril 2021; 115:1395-410). The GTS consists of a face sheet along with redacted laboratory results. Only carrier screening results are typically attached.

How is a suitability match using the results of a donor performed?

The carrier screening laboratory report attached to the GTS typically has a list of the genes/conditions screened for the donor. They can be compared against those screened for the sperm source. In general, if both gamete sources are carriers for the same recessive condition, the reproductive risk for an affected embryo/child would be increased to 1 in 4 chance (or 25%). If one gamete source is a carrier and the other has tested negative, or if both have tested negative, the reproductive risk would be reduced. Please see below for additional details on carrier screening.

It is highly recommended to work with a healthcare specialist like a genetic counselor or a fertility doctor to confirm a suitability match. Comparing carrier screening results can sometimes be challenging for the intended parents to do on their own for several reasons including:

* Laboratories may use alias names to refer to the same condition, such "Cystic Fibrosis" and "CFTR-related conditions."
* A gamete source may seem to be a non-carrier for a specific condition when their panel didn't include that gene/condition to begin with.
* For specific results, a carrier-carrier match may not always result in an increased reproductive risk for disease.

Fairfax EggBank's genetic counselor is available to help you with a suitability match. Please let your client services representative know that you are interested in one. A copy of the sperm source's laboratory issued carrier screening results would be required.

What happens if the match between a sperm source and an egg donor is not suitable?

There are several options you can consider:

1. Consider additional testing for the "discrepant" genes/conditions on the appropriate gamete source. For example, if the donor was not screened for a condition that the sperm source is a carrier for, we are happy to look into coordinating additional testing. Occasionally, additional testing may not be possible depending on the requested gene/condition.
2. Consider using the donor anyway while declining additional testing. Genetic counseling and informed consent would be recommended to understand the implications and risks, as well as a discussion with the managing IVF clinic to learn their policies in these scenarios.
3. Consider choosing a different donor.

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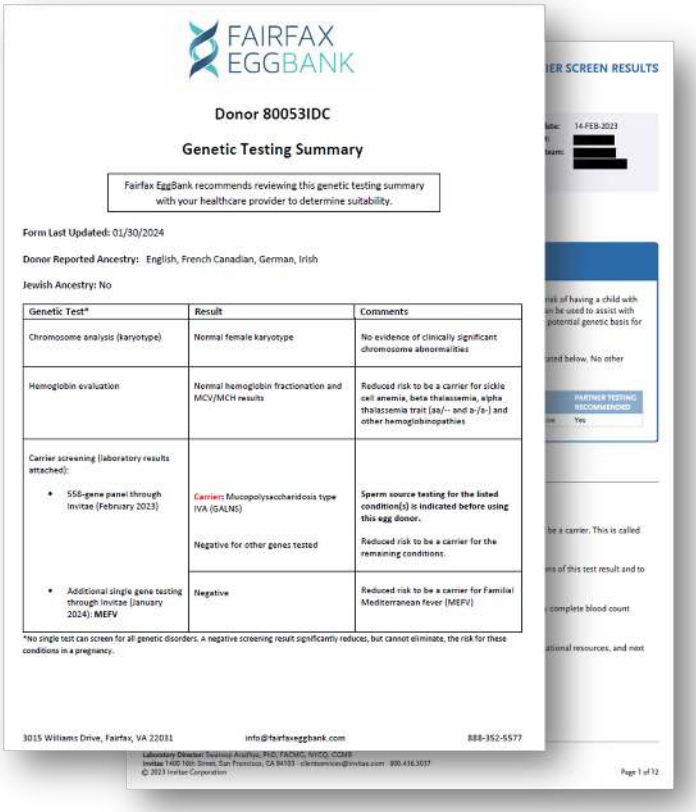
What are the components of a GTS?

Here is an example of what a GTS looks like. It will clarify the donor number, the reported ancestry, and the date it was last updated.

It will typically list 3 categories of genetic testing: chromosome analysis, hemoglobin evaluation, and carrier screening. The next pages explain these components.



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Donor 80053IDC

Genetic Testing Summary

Fairfax EggBank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Form Last Updated: 01/30/2024

Donor Reported Ancestry: English, French Canadian, German, Irish

Jewish Ancestry: No

Genetic Test*	Result	Comments
Chromosome analysis (karyotype)	Normal female karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Carrier screening (laboratory results attached):		
• 558-gene panel through Invitae (February 2023)	Carrier: Mucopolysaccharidosis type IVA (GALNS)	Sperm source testing for the listed condition(s) is indicated before using this egg donor.
	Negative for other genes tested	Reduced risk to be a carrier for the remaining conditions.
• Additional single gene testing through Invitae (January 2024): **MEFV**	Negative	Reduced risk to be a carrier for Familial Mediterranean fever (MEFV)

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

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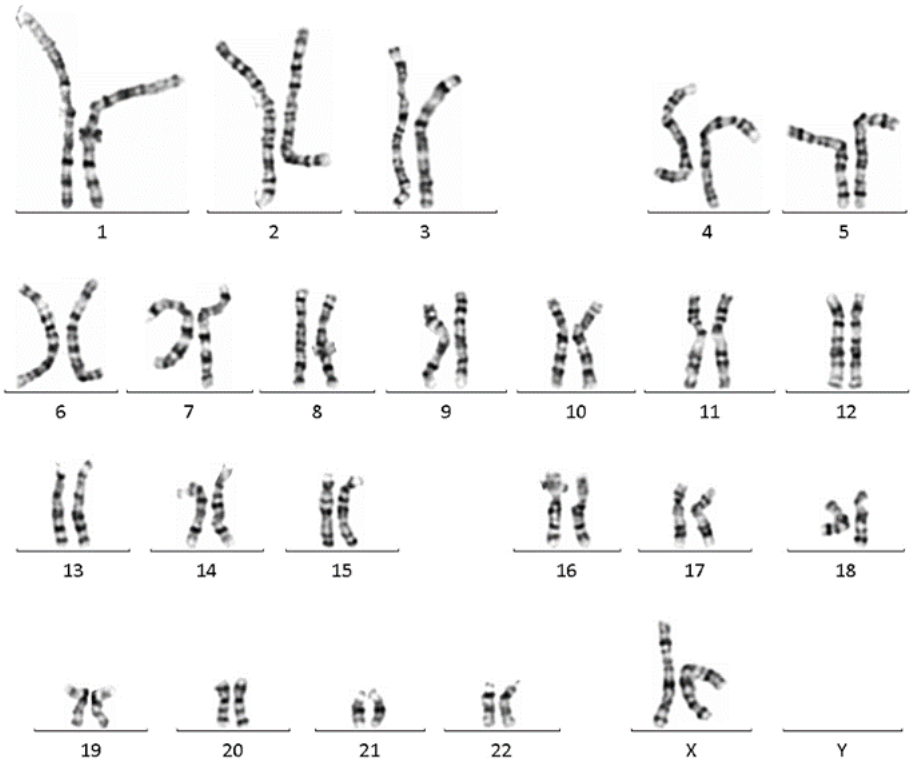
1. **Chromosome analysis (karyotype):** is an assessment of the donor's chromosome number and structure in a blood sample. Chromosomes are packaging structures for our genes, and we have 46 total chromosomes in most cells. As you see in the picture below, chromosomes look like "rods" under the microscope. They come in pairs with each set of 23 coming from each gamete source. Our chromosome pairs are labeled from 1-22, with the 23rd pair being the sex chromosomes, often known as the X and Y chromosomes. Individuals identified as females at birth will typically have XX, and males will have XY.

   Occasionally, there are structural rearrangements detected on a karyotype analysis that may increase the risk for aneuploidy (chromosome imbalance) in offspring. An example is a translocation, where two segments of two different chromosomes swap places. This may not lead to clinical symptoms for the individual who is a carrier for this rearrangement but may increase the reproductive risks for aneuploidy. Of note, there are a few structural rearrangements that are not associated with increased reproductive risks.

Note: A picture of a donor's karyotype analysis is not typically attached to the GTS.

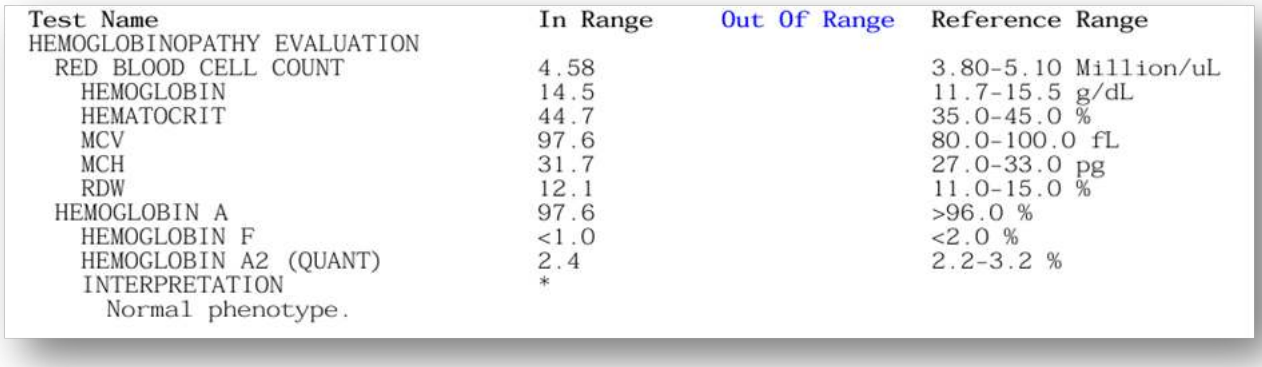


Normal female karyotype result: 46, XX

2. **Hemoglobin analysis:** is an assessment for several analytes in a donor's blood sample, like the volume of red blood cells and the level of hemoglobin (the protein that carries oxygen in blood). It is not a genetic test per se; however, it helps to assess the donor's chance to be a carrier for certain genetic conditions like sickle cell disease. The analytes that are summarized on the GTS are:

   * Mean corpuscular volume (MCV): an average size of red blood cells.
   * Mean corpuscular hemoglobin (MCH): an average amount of hemoglobin within red blood cells.
   * Hemoglobin fractionation: an assessment of the levels of different types of hemoglobin in blood.

   Based on the elevated or reduced amounts of some of these values, a carrier status for hemoglobinopathies may be suspected. Hemoglobinopathies are a group of genetic conditions that affect hemoglobin structure/function and may lead to severe anemia. Examples are beta thalassemia, alpha thalassemia, and sickle cell disease.



Test Name	In Range	Out Of Range	Reference Range
HEMOGLOBINOPATHY EVALUATION			
RED BLOOD CELL COUNT	4.58		3.80-5.10 Million/uL
HEMOGLOBIN	14.5		11.7-15.5 g/dL
HEMATOCRIT	44.7		35.0-45.0 %
MCV	97.6		80.0-100.0 fL
MCH	31.7		27.0-33.0 pg
RDW	12.1		11.0-15.0 %
HEMOGLOBIN A	97.6		>96.0 %
HEMOGLOBIN F	<1.0		<2.0 %
HEMOGLOBIN A2 (QUANT)	2.4		2.2-3.2 %
INTERPRETATION	*		
Normal phenotype.			

Of note, the carrier screening (see next) that a gamete donor gets also screens for the same types of hemoglobinopathies. Given how common a carrier status is for hemoglobinopathies in the general population, performing both forms of screening can identify the majority of carriers.

3. **Carrier Screening:** is a genetic screening test performed on the donor's DNA in a blood or saliva sample to assess her carrier status for hundreds of single-gene (monogenic) conditions. Being a carrier is very common in the general population; in fact, about 70-80% of individuals show positive results on these tests. Depending on the type of condition, most carriers of genetic diseases do not express symptoms.

   The main purpose of carrier screening is to assess reproductive risk for disease. By finding out the potential carrier status of egg and sperm sources, a suitability match can be performed.

   The types of conditions assessed by carrier screening for egg donors are either X-linked or recessive.

   X-linked conditions are due to mutations in genes on the X chromosome and typically affect males more severely. A carrier donor has a 50% chance for an affected male offspring. Therefore, donors who are carriers for X-linked conditions are not included in the donation program.

   Recessive conditions typically require both gamete sources to be carriers for there to be an increased reproductive risk. When both gamete sources are carriers for the same condition, there would be a 1 in 4 (or 25%) chance for each embryo/pregnancy to be affected. When one gamete source is a carrier and the other is not, the reproductive risk is reduced.

   We all have two copies of most genes, one coming from each gamete source. When our bodies make eggs/sperm, 50% of our genetic information is packaged into these cells. Therefore, a carrier of a recessive condition has a 50% chance to pass down their mutation.

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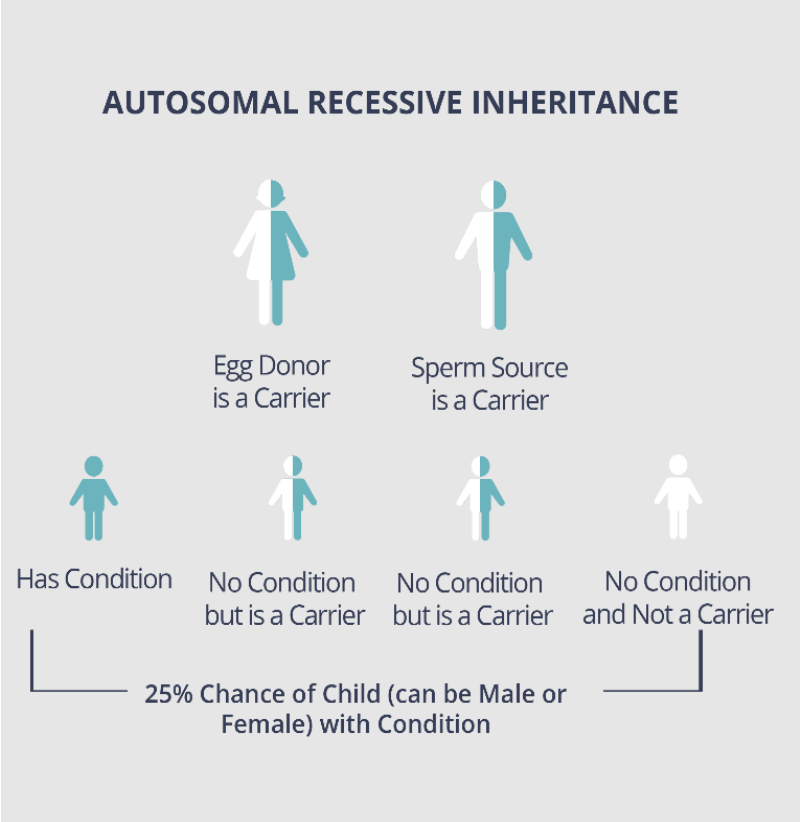
The figure below explains all 4 possible reproductive outcomes when an egg donor and a sperm source are carriers for the same recessive condition.



If you have questions about the GTS you received, please let your client services representative know. You may call 888-352-5577 or email info@fairfaxeggbank.com

ABOUT THE AUTHOR

Rawan Awwad, MS, CGC is a board certified and multi-state licensed reproductive genetic counselor with expertise in preimplantation genetic testing, carrier screening, and gamete donation. She currently serves as the Director of Genetic Counseling at Fairfax EggBank where she oversees the review and assessment of donor genetic testing, manages the investigation and dissemination of medical updates received on donors and donor-conceived persons, and serves as an in-house genetic expert for clients seeking suitability matching or clarification on donor histories/results. Prior to joining Fairfax EggBank, Rawan served as a Genetic Counselor at a PGT laboratory where she managed the review and counseling on PGT cases and served as a clinic liaison to referring clinics.