# WRITTEN SUBJECT INFORMATION

# Diagnostic testing supported by Genzyme Europe B.V. (“Sanofi-Genzyme”) on request of your treating physician

## Introduction

Your physician has reason to suspect you may be suffering from a **Lysosomal Storage Disorder** and you are being asked to give a blood sample to be able to confirm or exclude a possible diagnosis. Throughout the enclosed Informed Consent Form (ICF), “you” always refers to the person who is being asked to provide the blood sample for diagnosis.

The blood sampling and testing for one of the Lysosomal Storage Disorders is voluntary. It is important that you fully understand what it means for you when your blood is being tested. This information as well as the ICF describes what kind of testing will be done on your blood sample, what information will be collected, and what happens to the information. You should discuss any questions you may have with your physician.

If you sign the enclosed ICF, you agree your blood may be collected to help your physician to diagnose your disease.

## How can a Lysosomal Storage Disorder be diagnosed?

Lysosomal Storage Disorders are a heterogeneous group of diseases that originate when the lysosome is not functioning properly. Lysosomesare commonly referred to as the cell’s recycling centre because they process unwanted material into substances that the cell can utilize. Lysosomes break down this unwanted matter via enzymes. Individuals with a Lysosomal Storage Disorder have less than the normal amount of these enzymes or sometimes the enzyme is missing all together. When this happens, substances accumulate in the cell. In other words, when the lysosome does not function normally, excess products that would usually be broken down and recycled or removed from your cells, are stored in the cell. This may lead to different kinds of clinical symptoms.

To determine if you are missing one of these enzymes or have a reduced amount in your cells, a test can be done to measure the activity of these enzymes. This **enzyme activity laboratory test** can be done on a Dried Blood Spot (DBS) card. This is a type of blood sampling where blood is blotted and dried on a specific filter paper. To perform the test, only a few drops of blood are needed. For infants under 6 months of age, the blood sample can also be collected via a heel prick. Above this age, it is advised to collect blood from a vein, called venepuncture. For detailed information, please contact your physician.

On request of your treating physician, genetic analyses for Lysosomal Storage Disorder will be performed by ARCHIMED Life Science GmbH (“ARCHIMEDlife”), Leberstrasse 20/2, 1110 Vienna, Austria (contact: info@archimedlife.com), a specialized diagnostic laboratory that requires a patient consent form to be signed by the patient to perform any biochemical and/ or genetic analyses. Your physician will obtain a sample of your blood collected on a Dried Blood Spot (DBS) card to perform biochemical (enzymatic) testing for:

* - Fabry disease (Enzymatic testing: α-galactosidase A; Biomarker: Lyso-GL-3 (for females
* only), or
* - Pompe disease (Enzymatic testing: acid α-1,4-glucosidase), or
* - Gaucher and Niemann-Pick A/B (Acid Sphingomyelinase Deficiency, ASMD) disease
* panel diagnostics (Enzymatic testing: ß-glucocerebrosidase and acid sphingomyelinase), or
* - Mucopolysaccharidosis panel diagnostics (Enzymatic testing: α-L-iduronidase (MPS I),
* Iduronate-2-sulfatase (MPSII), N-alpha-acetylglucosaminidase (MPSIIIB), N-
* acetylgalactosamine-6-sulfate-sulfatase (MPS IVA), arylsulfatase B (MPS VI) and α-N-
* acetylglucosaminidase (MPS VII))

and, in case of a positive or borderline biochemical result, genetic analysis will be performed subsequently for either GLA (Fabry), GAA, (Pompe) GBA (Gaucher), SMPD1 (ASMD) or IDUA (MPSI), to determine if I am potentially affected with one of the above listed Lysosomal Storage Disorders. In case of a genetically confirmed result for Fabry disease, a Lyso-GL-3 analysis for male patients will be performed as well. In case of a genetically confirmed result for Gaucher disease, Lyso-GL-1 testing will be performed for both males and females to provide a baseline assessment.

## Role of ARCHIMED Life Science GmbH

ARCHIMED Life Science GmbH (“ARCHIMEDlife”) is a Medical Laboratory and Research Institute specialized in the detection and improvement of diagnostics of such rare disorders, and provides diagnostic testing from Dried Blood Spot filter paper cards for physicians and their patients around the world. Its goal is to improve the situation for individuals with rare disorders. ARCHIMEDlife is committed to protect the privacy of your health information including laboratory test orders and test results.

The DBS card will be sent to ARCHIMED Life Science GmbH (“ARCHIMEDlife”), Leberstrasse 20/2, 1110 Vienna, Austria (contact: info@archimedlife.com). The enzyme activity test will be performed in this specialized ARCHIMEDlife Medical Laboratory or in a subcontracting partner laboratory located at the Hamburg University Medical Center, Martinistrasse 52, Hamburg, Germany.

If the enzymatic testing shows a positive or borderline result, subsequent genetic testing (testing of hereditary material – genes) will be performed (only if a signed ICF is available) by ARCHIMEDlife to confirm or exclude a potential diagnosis of one of the Lysosomal Storage Disorders.

Your physician can track the status of the enzymatic and/ or genetic test and will notify you once he/she has received the results.

## What Information will be collected from your blood sample?

The following laboratory testing will be done on your DBS card:

* **Enzyme activity**

The enzyme activity assay is a test to determine the presence, absence or quantity of an enzyme’s activity on a specific substrate (material or substance on which an enzyme acts).

Enzyme

Substrate --------------------🡪 Product 1 + Product 2

Quantification of the products provides a measurement of the activity of the enzyme.

* **Genotyping**

Genotyping will be done to identify disease causing changes in your DNA (mutations) in a certain part of the gene possibly underlying your disease. Identifying the mutation(s) may be helpful in confirming your diagnosis, and also makes it possible to test at-risk family members. Only the specific gene that relates to the low or absent enzyme activity will be tested. No analysis will be performed on any other genes.

## Who is supporting this diagnostic testing?

## Role of Genzyme Europe B.V.

Genzyme Europe B.V. (“Sanofi-Genzyme”) supports the Diagnostic Services for Lysosomal Storage Disorders so that ARCHIMED Life Science GmbH can offer the services for free to physicians and their patients.

For statistical analysis, Sanofi-Genzyme receives the following data in an aggregated, fully anonymized form: origin of the sample (country and physician specialty), gender, which test is being requested and qualitative (positive/ negative) outcome of testing. For tracking purposes, Sanofi-Genzyme or representatives may provide logistic support whenever there is an explicit request from your treating physicians to ensure that sample material as well as the final medical report in the diagnostic service is delivered. To this end, the 8-digit Dried Blood Spot card ID as well as sample collection date, sample receipt date, sample status and result reporting date may be shared. All decisions impacting the management and treatment of your disease are the sole responsibility of your treating physician.

Sanofi-Genzyme is providing financial and logistical support so ARCHIMEDlife can provide these Diagnostic Services for Lysosomal Storage Disorders without any charge to you. The blood sample for diagnostic testing is collected by your physician and his/ her team. The hospital will not receive any payment for the collection of your blood sample nor for requesting the diagnostic testing.

All decisions in relation to the diagnostic testing and on the possible management of your disease are the sole responsibility of your treating physician and Sanofi-Genzyme will have no involvement in these decisions whatsoever.

## What steps will be taken to protect the confidentiality of your Information?

Care will be taken to protect your health information according to European, national and local privacy laws that apply. The **individual patient data** (first/ last name and date of birth) detailed on the DBS card will only be known and accessible to your physician and to the Medical Laboratories at ARCHIMEDlife and the Hamburg University Medical Center. The legal basis for processing your personal data is the signed Informed Consent Form.

## Data which is being shared with Sanofi-Genzyme

Only anonymized test results will be given in an aggregated form (combined with the results from other patients) to Sanofi-Genzyme for statistical analysis. Data which is being shared includes: the origin of the sample (country and physician specialty), gender, which test is being requested and qualitative (positive/negative) outcome of testing. For tracking purposes, Sanofi-Genzyme or representatives may provide logistic support whenever there is an explicit request from your treating physicians to ensure that sample material as well as the final medical report in the diagnostic service is delivered. To this end, the 8-digit Dried Blood Spot card ID as well as sample collection date, sample receipt date, sample status and result reporting date may be shared.

## How will you be informed about the outcome of the diagnostic testing?

Once data on enzyme activity and/or genetic testing are available, ARCHIMEDlife will make the results available to your physician via their online sample registration, tracking and reporting tool ARCHIMEDlife WEBPORTAL.

Your treating physician will then share the outcome of the diagnostic testing directly with you.

If a disease-causing characteristic mutation is found, it is usually highly conclusive.

In case no disease-causing genetic mutation is found, genetic changes responsible for the disease may still exist, and a disease can consequently not be fully excluded. Because of the complexity of genetic testing and the important implications of the test results, results will be reported only through a physician or genetic counselor. The results are confidential to the extent allowed by law.

## Will your physician be paid for requesting diagnostic testing on your blood sample?

Your physician and/or the hospital that employs your physician will not receive any payment from Sanofi-Genzyme for requesting the analysis. At the request of your physician, Sanofi-Genzyme offers the diagnostic tests without charge to your physician. Your physician is not obliged in any way to make use of these services and can also choose to arrange the testing in a different setting and cover for these separately.

## What happens to your sample and health information once the analysis has been performed?

* Data will be stored in the ARCHIMEDlife WEBPORTAL on secured servers located in Vienna, Austria. Your data will only be accessible to your treating physician.
* ARCHIMEDlife will retain your personal data for as long as this is necessary for the purpose of the biochemical and/ or genetic analyses of your sample.
* The personal data that ARCHIMEDlife collects from you will not be transferred outside the European Union.
* ARCHIMEDlife has implemented appropriate technical and organizational measures to secure the processing of your personal data.
* DBS card will be stored at ARCHIMED Life Science GmbH or by Hamburg University for 6 months and destroyed after this time frame.

## Storage and use of anonymized data for quality assurance and research

* You can help us to promote quality of testing and medical research for other patients. For the improvement and quality assurance of (future) diagnostic tests and medical research in which your data will only be used completely anonymously without any name or laboratory ID and no possibility to trace the data back to you, we only use the information age, gender and test result. The remaining sample material may be used for quality assurance and improvement for diagnostic testing as well as for research purposes to detect and find biomarkers.

## What are the risks to perform the diagnostic testing?

Blood used for the DBS card can be collected via a heel prick (for infants under the age of 6 months) or via venepuncture. About 1-2 ml will be collected. The blood will be taken by a qualified person. Risks include slight pain, bruising, redness, or a small risk of infection at the site of the puncture as well as general symptoms such as dizziness, fainting, or nausea. Please contact your physician for any further and detailed information.

## What are the possible benefits for your participation in this diagnostic testing?

Participating in this diagnostic testing can result in a potential diagnosis of one of the suspected Lysosomal Storage Disorders (when outcome of the diagnostic test is positive) or the exclusion of the suspected Lysosomal Storage Disorders (when the outcome of the test is negative). In some cases you may be asked to provide a second blood sample (when the outcome of the diagnostic test is inconclusive or borderline). If you have been tested positive for one of the suspected Lysosomal Storage Disorders, your physician will discuss with you the optimal management of your disease.

## Will it cost you anything to have these diagnostics test performed?

There are no costs for you to have your sample analysed.

## Will you be paid for diagnostic testing on your DBS card*?*

You will not be paid when you agree to diagnostic testing on your DBS card.

## Voluntary participation / withdrawal of participation

Collecting blood on a DBS card for diagnostic testing is voluntary. Even if you sign this form, you may stop the diagnostic testing at any time. Your healthcare and treatment by your physician will not be impacted by your decision to participate and/or withdraw, should you wish to do so. If you withdraw this permission, no additional analysis will be performed on your sample. You can withdraw your consent to the biochemical and/ or genetic analyses for Lysosomal Storage Disorder with future effect at any time either orally or in writing, without stating reasons. You have the right not be informed about the biochemical and/ or genetic test results (right not to know), to stop the biochemical and/ or genetic testing process at any time, and to request the destruction of all test results not already known to you already, and sample materials.

* What rights do you have when ARCHIMEDlife processes your personal data?
* You have the right to access and inspect your personal data;
* You have the right to ask for correction of your personal data if they are incorrect;
* You can ask ARCHIMEDlife to delete your personal data; (if there is no legal obligation to retain data);
* You can request that ARCHIMEDlife transfers your personal data to a third party;
* You can object to the processing of your personal data or ask for the application of restrictions;
* You have the right to receive a copy of all your personal data that are processed by ARCHIMEDlife;
* You can lodge a complaint about the processing of personal data by ARCHIMEDlife with the Data Protection Authority established in the EU member state in which you reside at any time;
* You have the right to withdraw the data collection and processing consent provided to ARCHIMEDlife under this consent at any time. Kindly note that a withdrawal of your consent does not affect the lawfulness of processing of your personal data based on your consent before the withdrawal.

## Who should you contact if you have any questions or problems?

Should you want further information regarding diagnostic testing, please contact your physician:

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| Family name, first name: |
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| Phone: |
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| Email |
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