

Fabry Registry Frequently Asked Questions

For People with Fabry Disease and Their Families





Table of contents

- ABOUT THIS BOOKLET4**
- I FABRY REGISTRY: GENERAL INFORMATION4**
 - What is a disease registry?4
 - What is the Fabry Registry?4
 - Why is the Fabry Registry important?6
 - Who can participate in the Fabry Registry?7
 - Is participation in the Fabry Registry paid?7
 - Why is my participation in the Fabry Registry important?7
 - Why are there multiple registries?.....7
 - Should I take part in more than one registry?7
- II FABRY REGISTRY: ENROLLMENT, INPUT AND PROCESSING OF DATA..... 8**
 - How do I participate in the Fabry Registry?8
 - What is the Patient Authorization and Information Form (consent form) and why is it important?8
 - Who will submit the data into the Fabry Registry?9
 - How often and for how long will my data in the Fabry Registry be updated?9
 - What is the patient QoL questionnaire?9
 - What happens to my data once they are entered?9
 - Who has access to my data?.....10
 - Are the data protected for patient privacy?.....10
 - Can I withdraw from participating in the Fabry Registry?11
- III FABRY REGISTRY: GOVERNANCE AND OWNERSHIP 11**
 - How is the Fabry Registry governed? 11
 - What is the role of Genzyme?12
- IV FABRY REGISTRY: OUTPUT..... 13**
 - Who analyzes and reports the data?13
 - How can I see my status?13
 - Are patients able to get the data from the Fabry Registry?13
 - How can I find the published outcomes?13
 - Where can I get more information about the Fabry Registry?13

ABOUT THIS BOOKLET

In this booklet, we answer questions that are frequently asked by people (and their families) who are participating or intend to participate in the Fabry Registry.

This booklet provides general information about the Fabry Registry and how it works, it gives practical information about participation and enrollment, and it explains what happens to data once they are entered in the Fabry Registry. It is intended to help affected individuals and their families to better understand the Registry.

The booklet does not provide information about the treatments available for Fabry disease, or the effects of treatment. For advice about medications or for help with any further questions you have about the Fabry Registry, please talk to your doctor or healthcare professional.

I FABRY REGISTRY: GENERAL INFORMATION

What is a disease registry?

A disease registry is a database that collects information on a wide population of individuals with a specific disease. Registries can have different goals, but mostly they are used for research in particular disease areas. Registries are very helpful in getting information on diseases and treatments, and are especially important in rare diseases. By definition, each rare disease has a small number of patients within any individual country, making it difficult to collect information about the signs and symptoms of the disorder in both treated and untreated patients.

What is the Fabry Registry?

The Fabry Registry is a large, ongoing, observational database with the aim of monitoring the long-term natural course of the disease and treatment outcomes. The Fabry Registry collects data from patients worldwide and will be maintained over a long period of time, thereby providing information that would ordinarily be difficult to obtain because the population would be too small.

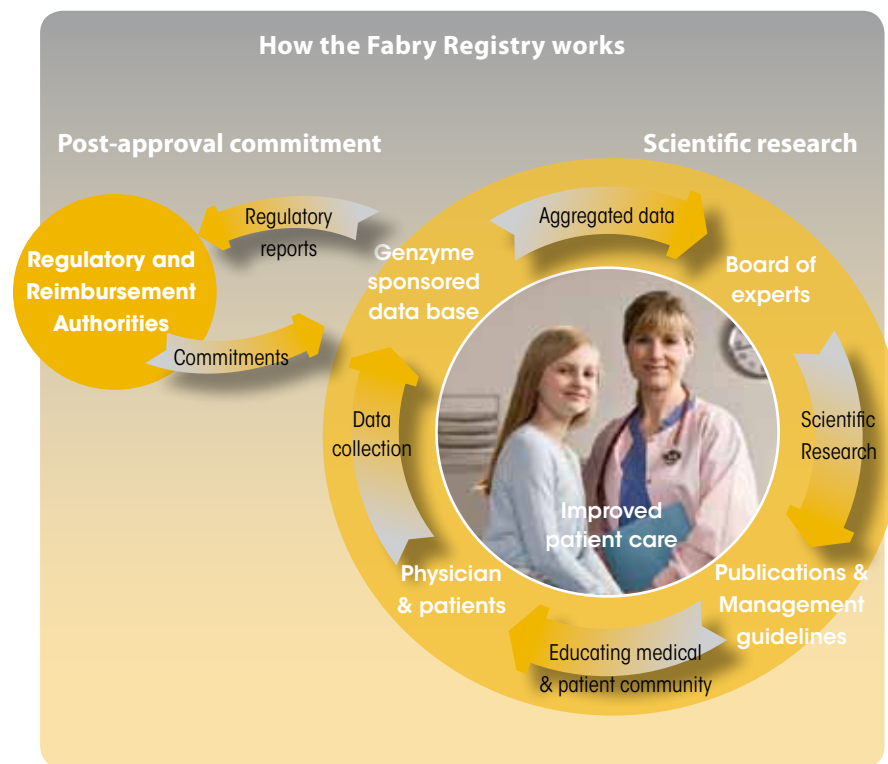
The aims of the Fabry Registry are to:

- determine the characteristics and progression of Fabry disease with and without treatment;
- establish if treatments are safe and effective;
- evaluate patient care;
- monitor patients' quality of life;
- create disease management and monitoring guidelines;
- improve understanding of the disease within the medical community.

The Fabry Registry contributes to the medical community's understanding of Fabry disease in several ways. For example, management guidelines and scientific publications developed by physicians who are participating in the Fabry Registry may lead to earlier diagnosis, more appropriate timing of intervention and, ultimately, better management of the disease.

This is especially important for patients with a rare disease, as knowledge about the disease and experience with therapies is limited. For example, if therapeutic goals are better defined, patients will also have a more accurate idea of what to expect from therapy, and whether they are reaching those goals.

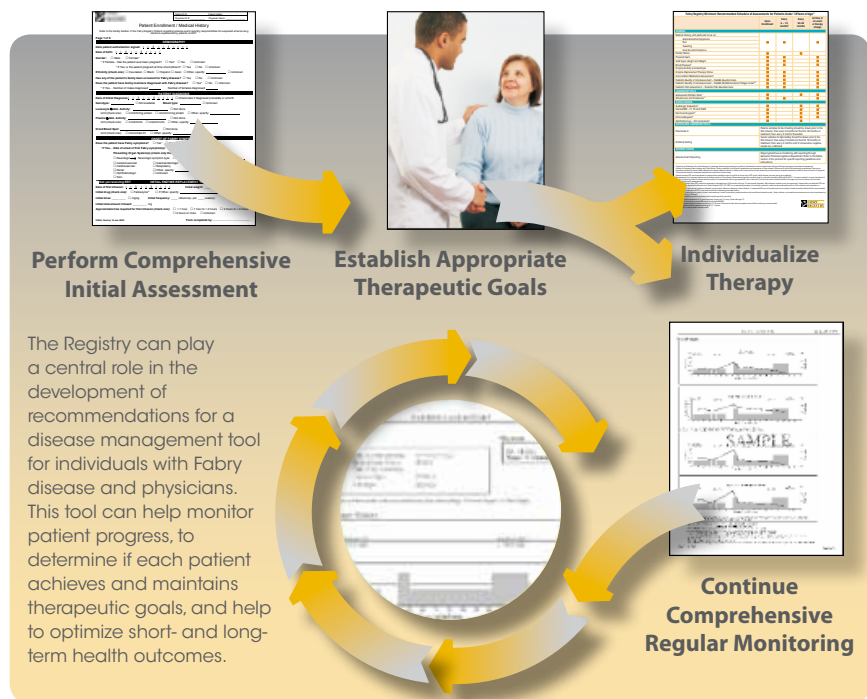
Part of the collective data is also provided to regulatory authorities such as the European Medicines Agency (EMA) and the United States Food and Drug Administration (US FDA) to fulfill post-approval commitments for enzyme replacement therapy.



Why is the Fabry Registry important?

The Fabry Registry has a number of potential benefits. These include:

- contributing information about the disease to the medical community, enabling development of recommendations to optimize patients' care. This can be achieved through publications and presentations at scientific conferences;
- collecting long-term data on a larger population of individuals – far more than is usually available in a clinical trial alone;
- providing insight on the disease, and especially long-term outcomes associated with safety and efficacy of the treatment. Regulatory agencies can monitor long-term patient outcomes of treatment(s) they have approved; often these agencies require the Registry to follow specific patient groups and to report the results annually.
- establishing links among doctors around the world. This can help to identify patients who may be eligible for clinical trials. This is particularly important in trials with patients who have rare diseases, due to the small numbers of patients and study centers worldwide;
- providing individual “patient case reports,” which can be printed from the Registry to help doctors and patients review status over time. The Fabry Registry can help both the people who contribute their data and the medical community.



Who can participate in the Fabry Registry?

The Fabry Registry is open to all people with Fabry disease, regardless of treatment status or treatment choice.

Is participation in the Fabry Registry paid?

You will not receive any payment or any other financial benefit as a result of submitting your data to the Fabry Registry. However, your individual report or the publication of Registry data may help your physician care for you.

Why is my participation in the Fabry Registry important?

Your participation in the Fabry Registry is crucial. For a registry to be effective, it needs to include as many people with as much data as possible, to improve the accuracy of the conclusions drawn from the data. Data from patients who are and who are not receiving treatment are equally important to enable research into the disease and the long-term effects of treatment. Without your help and cooperation, this partnership between patients and the medical community cannot succeed. Your participation in this program means that you will be helping science and research to gain better insight into the disorder, with the aim of improving the management of Fabry disease for every patient.

Why are there multiple registries?

Sometimes more than one registry on a specific disease exists. This can happen because registries are established by different stakeholders (scientists, industries, patient organizations, or governments), or because they have different aims. For example, one registry can monitor the medical problems experienced, while another might track the costs associated with a given disease. You may also hear about registries established on a national, regional, or international level.

Should I take part in more than one registry?

Registries can collect different kinds of information, and can enable data from a large number of people to be combined so that trends in disease progression, management, and treatment outcomes can be identified. Better insight into a disease can help physicians and researchers to improve your care and treatment. You may wish to discuss with your physician the feasibility of taking part in more registries to contribute to these endeavors.

II FABRY REGISTRY: ENROLLMENT, INPUT, AND PROCESSING OF DATA

How do I participate in the Fabry Registry?

Before you can participate, your physician needs to enroll in the Fabry Registry as a participating physician. Subsequently, your physician usually needs to obtain approval for the Registry from his/her hospital or center. The Independent Ethics Committee or Institutional Review Board of the hospital carefully reviews and evaluates all benefits and risks associated with the Registry before granting approval. Once your physician is enrolled, you will be asked to read and sign the Patient Authorization and Information Form. By signing this form, you authorize your physician to enroll your medical information in the Fabry Registry.

Before any data are entered into the Registry...

Physician submits protocol and patient authorization to Ethics Committee

Individual signs authorization

Individual can be enrolled

NOTE: You can always withdraw consent if you change your mind

Patient Authorization Form

PATIENT INFORMATION AND AUTHORIZATION
For release of Clinical Information to the
FABRY REGISTRY

Purpose and Background:
This form has been created to allow the release and processing of your (or your child's) medical information to the Fabry Registry, which is an observational registry program supported by the Genzyme Corporation. The goal of the Fabry Registry is to collect clinical data on people with Fabry disease in order to help us better understand the disease and its management.

The Fabry Registry was initiated in Europe at the end of 1998 and was revised for worldwide implementation in September 2008. The Fabry Registry will continue for a minimum of 5 years. The total number of people with Fabry disease who will participate in the Fabry Registry is difficult to predict as not all patients have been identified as well as possible. Initial sample population estimates are approximately 2,000-3,000 people with Fabry disease who potentially enroll in the Fabry Registry program. Clinical data that are reported to the registry include all of your (or your child's) Fabry symptoms, such as kidney and nerve laboratory results, organ assessments, pain evaluations, and quality of life assessments, will be submitted to the Fabry Registry database.

Benefits:
Fabry Registry findings may provide valuable information about Fabry disease and its medical management to your physician and other healthcare professionals. Since the Fabry Registry is an observational program, no experimental procedures are involved. Therefore, there are no medical risks to participants and there are no expenses to you for participating in the Fabry Registry.

Confidentiality:
Use of a patient identification number: Your (or your child's) identity, as well as any information obtained in connection with the Fabry Registry, will remain confidential and will not be disclosed except as described below. The Fabry Registry maintains confidentiality by assigning patient identification (ID) numbers—no identifiers are collected by the Fabry Registry. Your physician will be the only person who will know which ID number is assigned to you.

Individual patient authorization: Upon enrollment in the Fabry Registry Program, your physician will submit to the Fabry Registry your (or your child's) consent, date of birth (DOB), and gender along with specific clinical data as defined by the Fabry Registry protocol. Your physician will provide the Registry of your (or your child's) follow-up visits in past or future (or your child's) regular treatment program. After these follow-up visits, your physician will provide additional information to the Fabry Registry as submitted by the Fabry Registry protocol. In some circumstances, a member of Genzyme Corporation's Fabry Registry Center may visit your physician's office to collect the clinical information. Members of Genzyme Corporation's Fabry Registry Team and designated computer support staff, as well as representative from public health regulatory agencies (such as the Department of Health and Human Services or other national government agencies) may review the information submitted to and kept in the Fabry Registry. They will not, however, have access to your or your child's name. The Fabry Registry will provide a summary of your (or your child's) clinical information (identified by patient ID number, clinical gender, and DOB) to your (or your child's) personal physician to assist your physician in monitoring your (or your child's) treatment.

Version: 8 April 2008 1 of 2

What is the Patient Authorization and Information Form (consent form) and why is it important?

A Patient Authorization and Information Form (consent form) is a document to inform you about the purpose, risks, and benefits of participation in the Fabry Registry. It is important to read the consent form carefully, because it gives you all the information you need to know before you decide whether to participate. Your doctor will explain the consent form to you. Your signature represents your authorization for collection of your data.

Who will submit the data into the Fabry Registry?

If you and your physician agree to participate in the Registry, clinical information will be collected by your physician during your regular medical check-up. Your physician or nurse, or sometimes a data entry specialist with a confidentiality agreement, will submit your data to the Registry. It is recommended that assessments be conducted at least once a year.

How often and for how long will my data in the Fabry Registry be updated?

The Fabry Registry should be regularly updated with patient data - at least once a year - by all participating physicians. It should capture information from your regular check-ups. As the aims of the Fabry Registry include monitoring the long-term natural course of the disease and treatment outcomes, your information will be collected over many years. At any time, you have the right to withdraw from the Registry should you decide to do so.

What is the patient QoL questionnaire?

The Quality of Life (QoL) questionnaire asks a number of questions about your well-being. Over the years, researchers have developed several ways to measure the health-related well-being of people. One of these is the Short Form 36 (SF-36) questionnaire, which asks standardized questions about what you are able to do and how you feel. During a visit to your physician, you will be given this form to complete, usually at your annual check-up. It is very important that you take your time and answer all of the questions in the SF-36, because your data can only be used for research if all questions are answered.

QoL Questionnaire

The SF-36® Health Survey

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer that best describes you. If you are unsure about how to answer a question, please skip the question you see.

1. In general, would you say your health is:
 Excellent
 Good
 Fair
 Poor

2. Compared to one year ago, how would you rate your health?
 a. Excellent (better than one year ago)
 b. Good (about the same as one year ago)
 c. Fair (worse than one year ago)
 d. Poor (much worse than one year ago)

3. The following questions are about activities you might do during a typical day. Over your health now (mark you in these activities if you have trouble):

ACTIVITIES	Yes, a lot	Yes, some	No, not at all
a. Vigorous activities, such as running, lifting heavy objects, pushing or pulling, or strenuous sports	-	-	-
b. Moderate activities, such as carrying or lifting heavy objects, climbing stairs, pushing or pulling, or digging	-	-	-
c. Lifting or carrying groceries	-	-	-
d. Climbing several flights of stairs	-	-	-
e. Walking one block	-	-	-
f. Walking several blocks	-	-	-
g. Walking one mile	-	-	-
h. Walking several miles	-	-	-

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any physical health problem?
 a. Cut down on the amount of time you spent at work or other activities
 b. Accomplished less than you would like
 c. Missed or had to be absent from work or other activities
 d. Done anything particularly hard or difficult (for example, it took extra effort)

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or nervous)?

PROBLEMS	Yes, a lot	Yes, some	No, not at all
a. Cut down on the amount of time you spent at work or other activities	-	-	-
b. Accomplished less than you would like	-	-	-
c. Missed or had to be absent from work or other activities	-	-	-
d. Done anything particularly hard or difficult (for example, it took extra effort)	-	-	-

6. During the past 4 weeks, to what extent have your physical health or emotional problems limited only your normal social activities (such as family, friends, neighbors, or groups)?

PROBLEMS	Not at all	A little	Quite a bit	A great deal
a. Family	-	-	-	-
b. Friends	-	-	-	-
c. Neighbors	-	-	-	-
d. Groups	-	-	-	-

7. During the past 4 weeks, how often have you had any of the following problems?
 a. Pain (aches, pains, stiffness, or soreness)
 b. Headaches
 c. Dizziness
 d. Fatigue
 e. Shortness of breath
 f. Trouble sleeping
 g. Trouble concentrating
 h. Trouble remembering things
 i. Trouble with your vision

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What happens to my data once they are entered?

After entry, your data are made anonymous by using your initials and your date of birth to create a Registry ID that is stored securely. Each year, your physician will update the clinical data that were collected during your regular medical check-up, so that your own data can be followed over a number of years. Once data are entered, they are available for larger analyses. These are performed when a physician requests

certain information from the Registry. For example, a physician may ask for “data of all adult patients with pain in their stomach, selected in age groups 20-30, 30-40, and 40-50 years.” The details provided are “aggregate” data on a number of patients who fulfill the criteria for the analysis, and will be examined for important information that may have an impact on your disease management. Analysis of aggregate data from the Fabry Registry may be published or presented within the medical community, with one aim to share knowledge and to improve patient care and management of the disease.

Who has access to my data?

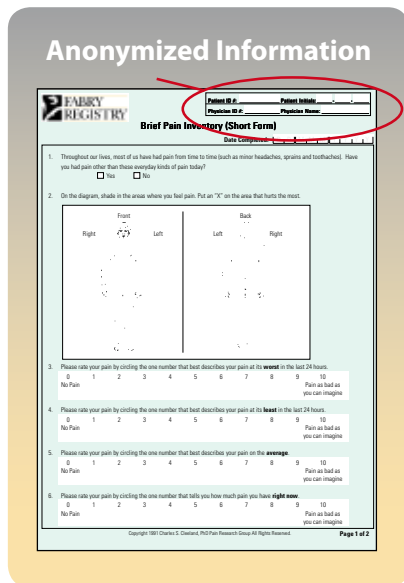
Your physician will have access to your personal data. He or she may also give authorization to the nurse or data entry specialist who is entering the information in the Fabry Registry. By consenting to participate, you enable your physician to use the Registry to monitor your individual medical condition over time.

Your anonymized information that has been entered into the registry can be viewed by designated Genzyme Fabry Registry team members, for example, a data manager, a trainer, or a programmer. The data manager and trainer make sure that your data are complete and correctly entered, and they help to answer questions about the database from your physician or data entry nurse. The programmer has to ensure that the data are properly prepared for analysis.

Representatives from public health regulatory agencies such as the EMA and the FDA may also review collective data from the Fabry Registry. In some particular cases, national agencies may ask for individual data, which can be given only by a physician. Nonetheless, in all cases, only your physician will know your personal information.

Are the data protected for patient privacy?

There are strict consent and privacy regulations under the Health Insurance Portability and Accountability Act (HIPAA) that ensure confidentiality. Data that are entered in the Fabry Registry are anonymized by removal of obvious identifiers such as name or address. All patients are referenced by a Registry ID number only. Your individual data will not be made available to employers,



educational institutions, your spouse, children, or anyone else in your family. Your physician is the only person who will be able to identify your data. Only anonymized data could be shared with national regulatory or reimbursement agencies, at their request.

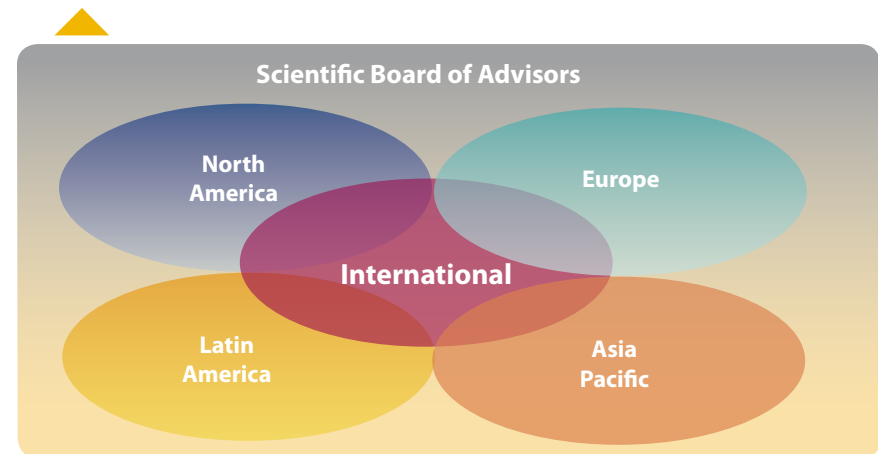
Can I withdraw from participating in the Fabry Registry?

Your participation is voluntary. You have the right to withdraw from the Fabry Registry at any time and can do so through communicating this decision to your physician. He or she will then withdraw you from participating in the Fabry Registry. As noted in the Patient Authorization and Information form, if you withdraw from the Registry, Genzyme will remove your (or your child’s) personal ID number and initials. The clinical data will remain in the database for use in aggregate data reporting. Genzyme will maintain in its database only previously authorized data, and only in a de-identified form.

III FABRY REGISTRY: GOVERNANCE AND OWNERSHIP

How is the Fabry Registry governed?

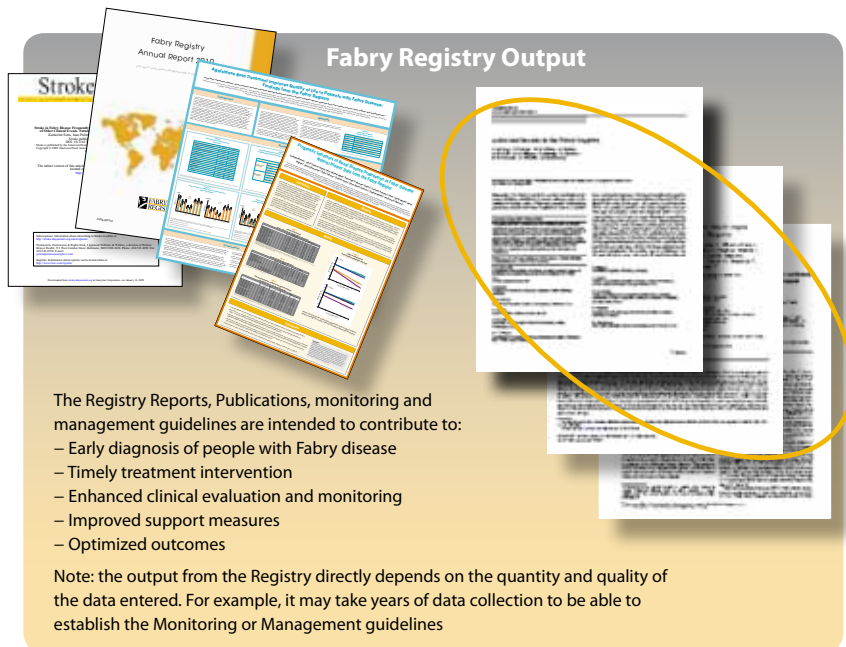
The Fabry Registry is governed by Boards of Advisors, independent groups of physicians who have extensive scientific and clinical expertise in the field of Fabry disease. There is an International Board of Advisors, but regional boards also serve Europe, North America, South America, and the Asia-Pacific region. These boards oversee analyses of the information in the Registry, and frequently publish analyses of the Registry data to educate the medical community. No data from the Fabry Registry can be published without review and approval from the applicable Board of Advisors.



What is the role of Genzyme?

Genzyme sponsors the Fabry Registry maintenance, and supports the data collection, data management, statistical analyses, and regulatory review under many of the same strict operating procedures used for clinical trials, and in compliance with local and international privacy regulations. Genzyme also provides administrative support to the Boards of Advisors worldwide.

As Genzyme is experienced in the development of therapies for rare diseases, the company sponsors registries for these conditions because registries have been proven to be very useful.



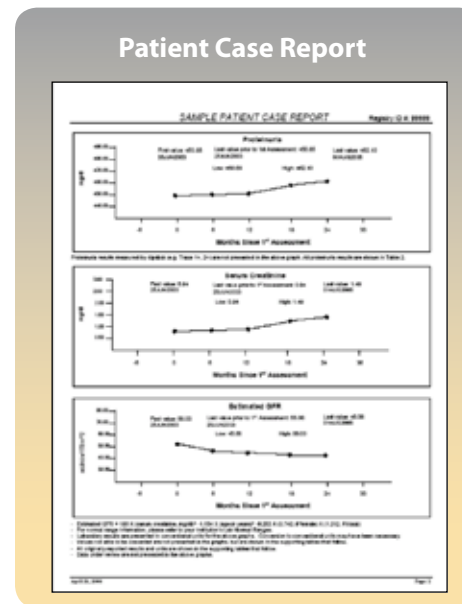
Fabry Registry Output

The Registry Reports, Publications, monitoring and management guidelines are intended to contribute to:

- Early diagnosis of people with Fabry disease
- Timely treatment intervention
- Enhanced clinical evaluation and monitoring
- Improved support measures
- Optimized outcomes

Note: the output from the Registry directly depends on the quantity and quality of the data entered. For example, it may take years of data collection to be able to establish the Monitoring or Management guidelines

IV FABRY REGISTRY: OUTPUT



Who analyzes and reports the data?

Data can be analyzed and reported at periodic time points as well as upon specific request by the medical community. Physicians are encouraged to collaborate, share observations, and generate hypotheses for evaluation.

How can I see my status?

Your physician will regularly enter the outcomes of your medical check-ups in the Registry. Over time, enough data should be entered to provide an overview in the form of a summarized report of your clinical status. Your physician

may request a report on your status from the Registry, and your physician may share this with you.

Are patients able to get the data from the Fabry Registry?

Your physician is the only person who can give you information about your own medical data from the Registry. In addition, further information that has been gathered in the Fabry Registry about people living with the disease and the different medical problems they encounter will be available in the “Fabry Registry Annual Report for People with Fabry Disease and Their Families.” Talk to your physician about this.

How can I find the published outcomes?

Scientific publications are accessible to everyone. Publications from the Fabry Registry are made available to the participating physicians. You can ask your physician for more information about the published data.

Where can I get more information about the Fabry Registry?

For additional information about the Fabry Registry, contact your physician.

