# Roche Specimen Repositories - Frequently Asked Questions

## 1. What is a Specimen Repository?

A specimen repository, also known as a biobank, collects, stores, processes and distributes (according to appropriate laws, rules and regulations) biological materials and the data associated with those materials. The purpose can be scientific research or medical treatment. Typically, "biological materials" are human samples – such as tissue (including organs) or blood and other body fluids, as well as substances extracted from these samples – and "data" is any information – including medical – pertaining to the donor of the specimen. A specimen repository can also include tissues from animals or plants, cell and bacterial cultures or environmental (soil, water) samples.

Specimen repositories exist within a variety of institutions, such as academic medical institutions, and pharmaceutical and biotechnology companies. They can also be stand-alone organizations, including independent companies (both for-profit and non-profit) that can provide repository services and access to samples as a service the research community or patients.

Modern specimen repositories that support research are highly complex in their operations, and often represent large, specialized organizations comprised of individuals with expertise spanning biology and pathology, bioinformatics and information technology applications and infrastructure, laboratory and logistic operations, and law and ethics. Specimen repositories must remain committed to the rights of the tissue donors, while simultaneously serving the needs of biomedical researchers.

Among the specimen repository's activities are:

- **Recruiting donors** and supporting them through the **informed consent** process. Such recruitment also involves coordination with ethics review boards to design protocols that provide the full scope of donor protection.
- Interfacing with the clinical setting to **collect specimens** during various participants' visits and getting those materials to the repository. Similarly, the specimen repository provides systems and support to collect the donor's **clinical and other information** from the medical record and from the patient or doctor interviews and other sources. This information is then formatted for secure storage (either as hard copy or, generally, in electronic form).
- Operating a specimen repository with full **logistical support**, including appropriate collection systems, transportation, various types and temperatures of storage capability, pathology review, and procedures to receive, manage, and distribute specimens.

- **Supporting processing laboratories** that can carry out steps needed to preserve samples and/or extract molecular components from them (such as DNA and RNA) and add these derivatives to the repository's inventory.
- **Providing scientists with traceable access** to the inventory of specimens and data at the level of identity protection specified in the informed consent so that they can curate the specimen repository and/or request materials that support their research protocols according to protocol and informed consent wordings.

## 2. Which categories of specimen repositories do exist and which are their goals?

There is currently no universally agreed-upon or used classification system for specimen repositories, although distinctions along several categories are commonly mentioned:

- **By intended use:** Use for research only, or as a source for therapeutics: most repositories currently fall into the first category, but there are emerging examples for the second, such as umbilical blood/stem-cell repositories stored for individual or community use.
- **By the group of participants targeted and by size:** Repositories may focus on very specific, narrowly defined groups of participants (e.g. with a certain rare disease) and be thus quite limited in size. If many such smaller studies are maintained in one repository, then the size (and usefulness) of such a repository may of course become quite large. Other repositories are designed to collect a broad, cross-sectional, representative sample of the population at large at a national or supranational level, and may thus be of very large size (also referred to as "population-based repositories" e.g. the UK BioBank which intends to collect specimens from ½ million participants).
- **By retrospective or prospective design of study:** retrospective collections are generally case-control collections addressing specific biological or medical question (e.g. from patients suffering from a certain disease, and unaffected controls), with no future collection of additional specimens or data planned; prospective studies follow participants in an ongoing ("longitudinal") fashion, collecting additional data and/or tissues as time passes (this is important as prospective studies cannot anonymize specimens – see below).
- **By nature of specimen:** in as much as early specimen repositories were often focused on blood samples for DNA analysis (genetics), increasingly a more comprehensive view of biomarker-relevant specimens is embraced that includes various other tissues and body fluids, as well as analysis of mRNA (gene expression), proteins, metabolites and other molecules.
- **By the entity accountable for the repository:** these may be academic institutions such as universities or research institutes, pharmaceutical, diagnostics, or biotechnology companies which collect samples for their own research use, or stand-alone organizations created explicitly for the purpose of setting up and maintaining

specimen repositories, such as the UK BioBank, or companies which commercially distribute specimens.

### 3. What specimen repositories does Roche maintain and for what purpose?

Both the Pharmaceutical and the Diagnostic Division of Roche collect specimens for research. **In Pharmaceuticals**, Roche collects specimens as part of clinical trials for new drug development, with a particular interest in identifying characteristics ("biomarkers") that may predict, among various parameters, whether a patient is likely or not to respond to a new drug, or to develop a side effect or not. **In Diagnostics**, the research interest focuses on identifying and assessing new tests for being at risk for a disease (so it may be prevented), for detection of a disease in its early stages when treatment is more likely to be successful), and for understanding the outlook (prognosis, good or bad) of a disease once it has occurred.

### 4. How long are specimens maintained in Roche repositories?

The duration of sample maintenance depends on the intended use and is generally specified in both the research proposal that is approved by Ethical Committee review and in the informed consent. Some samples that are collected for a very specific purpose may only be kept until this purpose has been achieved; others are collected for longer-term storage (often for up to 15 years, as this is the time for which Roche is obliged to keep all records of a drug research-and-development project) or even indeterminately. Once the decision is made to remove specimens from the repository, they are destroyed, whereas data may continue to be retained.

### 5. Where do population-based repositories exist?

National population-based repositories exist, or are being developed, in Estonia, Canada, Iceland, Japan, Latvia, Singapore, Sweden and the United Kingdom. These large repositories range in size, seeking from 60,000 to as many as a million volunteers. Most of them are public population-based repositories, managed in partnership with the appropriate national government.

### 6. Is a specimen repository the same thing as a patient registry?

No, a specimen repository is not the same thing as a patient registry, but they can be quite complementary as they contain information that can be mutually helpful while conducting research. A specimen repository will contain mostly human tissue samples, as well as a variety of body fluids. A patient registry will have information and data on patients, patient populations, patient groups and sub-groups as well as general health care information, mortality and hereditary data.

Information between a patient registry and a specimen repository can usually only be shared following patient consent.

## 7. How many specimens are needed for a repository?

The number of specimens necessary depends on the research question that scientists seek to answer. All medical research results depend on appropriate statistical analysis, and to arrive at conclusions that are reliable and not likely to coincidence or chance, it is always necessary to examine a number of research subjects in each group. This will allow the identification of shared or common, characteristics, such as a biomarker that is typical for a disease. Generally, the more complex a question asked is, the larger the group of research subjects (cases and controls) will need to be. Commonly, study sizes range from less than 100 to many thousand human subjects. A repository that contains samples from a number of such studies may therefore reach a very considerable size.

## 8. What are the constraints to the research that may be done?

Whenever individuals provide specimen for a repository, they are asked to explicitly consent to the use of their specimens for particular purposes. The consent may be limited ("narrow") to the sample being used to investigate a single specific disease area and the associated drug, or a specific biological test, or it may be more encompassing ("broad"), permitting the use of the specimen for a number of purposes, investigating any biological marker, for any disease, at any time in the future. Most commonly, a sensible compromise between very narrow and very broad consents is used, providing both optimal use of the specimen for research and consideration of the donor's autonomy. The nature of the consent provided defines the research that may be performed.

## 9. Who will be able to see information held in a repository?

Participants donating tissue or body fluid to a specimen repository should always be told, as part of the informed consent process, who will have access to which parts of the information about them, and to what degree their identity will be protected.

At Roche, all specimens and information are coded, and Roche has no access to the actual entity of the donor. However, the physician ("clinical investigator") must be able, for reasons of safety, to trace the code to the respective individual, as long as the trial is in active progress. Some specimens, where particular concerns regarding donor confidentiality apply, are re-encrypted with a second code ("double-coded") to provide even greater security; and sometimes the link to this second code may be destroyed to permanently make any tracing back to the donor impossible ("anonymization").

All studies carried out on repository specimens are analyzed as groups of samples only, thus precluding any attribution of results to individual samples or identification of individual donors. For the same reason, as a rule, information on an individual's test result is also not

provided back to the participant. In addition, since most of the research conducted is at an early stage being often still exploratory, such data may not be used for any medical decisions.

### 10. Will participation in the Roche repository affect their health insurance?

Since this information is strictly confidential, and since it is coded (or double-coded), it also can not accidentally be disclosed. In Europe as well as in the U.S., data privacy regulations would prohibit such a transfer of information anyway. Participants need not be concerned in this regard.

### 11. Will law enforcement agencies be able to get access to Roche repository data?

This is not possible for the same reasons as pointed out above in question 10.

### 12. Can sample/s be withdrawn from the specimen repository after they have been included in the repository?

Only if samples have been anonymized is a withdrawal from a repository no longer possible. In all other circumstances (coded, double-coded samples) a withdrawal of both specimen and data is possible at any time upon the participant's request. All future analyses will then be carried out without the patient's sample; however, analyses already completed will not be modified (i.e. continue to contain the participant's information as part of the overall result).

### 13. Can someone say no to particular types of research?

This should be discussed when the consent to donating a sample to the repository is given, but it is likely that honouring such requests will be too complex for the specimen repository's operation, and it will therefore usually mean that one should not participate altogether.

### 14. Will participants be told about the results?

For reasons of data protection and confidentiality, repository samples are coded or double-coded, precluding direct communication of individual results back to the patient. This will have been explained in the informed consent. In addition, since most of the research conducted is at an early stage, the medical significance of such tests is still mostly unclear, and it would be difficult or impossible to advise the participant of the meaning of the result.

### 15. What happens if Roche finds out that the human subject has a problem as a result of doing the research? Will be the human subject told? What if the human subject doesn't want to know?

This should be discussed when the consent to donating a sample to the repository is given, because, as a rule, the results are not conveyed back to the participants.

### 16. Is it safe to contribute to the Roche repository?

The only potential health risks from participating in the Roche specimen repository would be the result of a mishap associated with the procedure of specimen collection. Even the donation of a single blood sample can carry a very remote risk of injury, resulting in local tissue damage, and with any skin puncture carries the remote chance of an infection being introduced into the body.

### 17. What is the information process?

Once donors have provides a sample, they will likely not hear anything more, although one day, the sample may have helped contributing to a new medical finding or treatment that is reported in the media.

### 18. What if patients want to join a clinical trial, but not give a sample to the repository?

When patients provide the informed consent, they will be given the opportunity to agree on participating in the repository or to decline such participation. If participation will be of such importance to the trial, then declining to provide a sample would likely make it impossible for the patient to join that trial.

### 19. Do other pharmaceutical companies have specimen repositories?

Yes, many pharmaceutical as well as diagnostic companies maintain repositories similar to the one at Roche, for the same purposes and with similar guidelines and safeguards. Most companies, like Roche, believe that access to these specimens has the potential of providing insights that would make new drugs more effective and safer. Thus, they feel a scientific and moral obligation to avail themselves of this opportunity.

### 20. Does Roche obtain samples from public sector repositories?

Some repositories make their samples and/or data available to any interested researchers, be they from the public or commercial sector. It is also possible that the public sector specimen repository will charge company researchers a fee for having access to their samples and/or data.

### 21. Will being in the Roche specimen repository given any direct benefit such as better medicinal care or a financial reward?

The donation of a sample to a specimen repository is always voluntary and undertaken for altruistic rather than for financial motives, namely to help move research along and ultimately make progress in creating better medicines. Generally, donors will be reimbursed for expenses incurred, such as travel costs and/or time off work, but there will not be any further direct benefit in terms of treatments. The hope is that new knowledge can be reached through research on samples related to disease causes and future treatment options.

### 22. How can someone learn more about their eligibility to participate in the Roche repository?

Generally, one will be asked directly to participate in this research by the health care provider, most commonly in the context of participating in a drug trial or other clinical research to which the potential donor is contributing.