



## **SCNIR EUROPE**

Severe Chronic Neutropenia International Registry  
European Office

SCN International Registry, European Office  
Hannover Medical School  
Carl-Neuberg-Str. 1  
D-30625 Hannover  
Germany  
Tel.: +49-511-557105 FAX: +49-511-557106 e-mail: [SCNIR@mh-hannover.de](mailto:SCNIR@mh-hannover.de)  
[www.severe-chronic-neutropenia.org](http://www.severe-chronic-neutropenia.org)

---

### **PATIENT INFORMATION** FOR PARTICIPATION IN SCNIR AND BIOBANK

We would like to cordially invite you as a patient or as a parent or legal guardian of a minor patient to participate in our registry for severe chronic neutropenia. In the following, this information sheet summarizes the main aspects of the Severe Chronic Neutropenia International Registry (SCNIR), as well as the conditions for participation in the SCNIR biobank. If you understand the principles of the SCNIR and the SCNIR biobank and you or your child wish to participate, we ask you to confirm this by signing the consent form.

#### **Severe chronic neutropenia**

The term "severe chronic neutropenia" describes a group of different diseases whose common feature is a persistent reduction in absolute neutrophil counts (ANC) to less than 500 /  $\mu\text{l}$  associated with an increased susceptibility to infections. The white blood cells (leukocytes) are responsible for the defense against infections. The main task of the largest leukocyte subgroup, the neutrophil granulocytes (also called "neutrophils"), is the defense against bacteria. Therefore, individuals with neutrophil counts below a certain normal level are at risk for bacterial infection. Causes of severe chronic neutropenia may be congenital or acquired. In the meantime, numerous different genetic defects are known as the cause of congenital neutropenia.

Today's knowledge on the underlying mechanisms of severe chronic neutropenia are mainly due to the establishment of the SCNIR. In close cooperation with research laboratories and the increasingly improved techniques of molecular biology, knowledge about the biology of the various forms of the disease has been continuously improved by research.

## **Section I: Information on participation in the SCNIR**

### **Key objectives of the SCNIR are:**

- Documentation of the long-term clinical course of severe chronic neutropenia and any disease presenting with chronic neutropenia (e.g., Shwachman-Diamond syndrome) for the evaluation of disease progression and therapy.
- Evaluations on the occurrence, development and prognosis of disease-related concomitant or secondary diseases, such as osteoporosis, spleen enlargement, reduction of other blood cells, chromosomal abnormalities, myelodysplastic syndrome (MDS) or leukemia.
- Establishment of an international network of hematologist and pediatricians and other treating physicians to steadily increase their knowledge of severe chronic neutropenia.
- The expansion of the existing demographic database for further scientific evaluations with the aim of improving the diagnosis and treatment of severe chronic neutropenia.
- Documentation of patient pregnancies to better assess potential risks to parents and newborns, and to develop current family planning recommendations.

### **Structure of the European arm of the SCNIR**

The European branch of the SCNIR is divided into the data center at the Hannover Medical School, headed by Dr. med. Cornelia Zeidler, and the research laboratory with a biobank for patient samples, which is located at the University Hospital Tübingen and directed by Prof. Julia Skokowa and Prof. Welte. In addition, the SCN Registry maintains close contact with physicians in most European and some non-European countries, who are recognized as experts in the area of severe chronic neutropenia.

### **We would like you to know the following about participating in the SCNIR**

1. Participation in the SCNIR is completely voluntary. Non-participation will not affect your further medical treatment.
2. By refusing to participate or leaving the SCNIR, you / your child will not suffer any disadvantages.
3. Your data will be stored and processed in pseudonymised form on the server of the data center of Leiden University and the Hannover Medical School, in accordance with the data protection laws.
4. A termination of study participation is possible at any time without giving reasons. In the case of a withdrawal, you can decide whether your data should be deleted or used in anonymous form for the study.

## Admission criteria for the SCNIR Europe

You / your child can be enrolled in the SCNIR Europe because you / your child has been diagnosed with severe chronic neutropenia.

The **following information is required** from each patient for inclusion in the SCNIR Europe

1. All available **blood counts** showing that the absolute neutrophil count (ANC) was at least three times less than 500 /  $\mu\text{l}$  prior to admission (in patients with frequent infections below 1000 /  $\mu\text{l}$ ).
  2. A **bone marrow** finding confirming the diagnosis of "severe chronic neutropenia"
  3. A **cytogenetic evaluation**, if the patient is treated with G-CSF (Neupogen®, Lenograstim® or other preparations) or if treatment is already planned.
  4. A positive antibody result for autoimmune neutropenia.
  5. The agreement signed by the patient himself. For patients under 18 years of age together with the patient's legal guardian.
- Exception are: patients suffering from **Shwachman-Diamond syndrome (SDS), type Ib glycogenosis (GSD Ib), Barth syndrome** or **any other condition** in which neutropenia is a major symptom of the disease. These patients can be enrolled regardless of their neutrophil count or other blood cell counts.
  - Patients with cyclic neutropenia, in whom a cycle of at least three blood counts per week must be documented for four to six weeks.

## Data collection

For inclusion in the SCNIR, we may require written consent from you and, if applicable, a parent or guardian to read medical reports, and to request and document medical reports from the treating physicians. If the retrieval of findings with the attending physician should not be possible after registration at any time, e.g. after a change of doctor which has not been communicated to the registry, we also ask for your consent to contact you directly in this case to ask you for your current doctor or current findings. If you agree, please check the relevant section in the consent form and enter your current email address for contact.

For registration in the registry and the annual follow-up, the following information will be requested from you and/or your treating physician:

- Infection frequency and type of infections before and at the time of admission, as well as the respective annual interval after admission
- Size, weight, stage of development, clinical findings (such as liver and spleen size)
- Treatment details (name of the drug (s) used, dosage)
- Duration of treatment with date at start and end, reasons for therapy changes.
- Family history (other patients in further relationship with indication of degree of relationship)

In addition, the following findings are documented:

- Bone marrow findings
- Chromosome analysis of bone marrow cells (cytogenetics)
- Human genetic findings
- Blood pictures (if possible also before therapy start)

For inclusion in the SCNIR, it is not necessary to be a patient at the Children's Hospital in Hannover.

### **Data storage and processing**

The SCNIR maintains two data collection centers worldwide that collect and process clinical information from registered patients. The European data center is located in Hannover, the US data center for the US, Canada and Australia in Seattle, Washington. Each of these centers is in close contact with scientific laboratories, where relevant diagnostics are carried out to confirm the diagnosis and classification of the disease, as well as research laboratories in which patients' material is stored (see section II on the biobank form) and relevant research projects on various aspects of severe chronic neutropenia. In addition, there are cooperations with the EWOG-MDS study (reference morphology of the bone marrow) and other research laboratories, depending on the research question. The research results are linked to the clinical data for scientific evaluation. The personal data on the declaration of consent are stored separately from the registry documents.

Publications and presentations of collected data in scientific journals or at scientific meetings will include data only in anonymous form, which means without patients' names. Furthermore, the SCNIR will not share any data resulting from your participation in this research project without your prior written consent.

### **Privacy**

The SCNIR manages patient data in accordance with the applicable data protection regulations, in particular the General Data Protection Regulation (DSGVO) of 25 May 2018. You have the right to information about the stored personal data concerning you (article 15 DS-GVO). If you discover that wrong data is being processed for your person, you can request a correction or a specific supplement (Art. 16 DS-GVO). You have the right to request the deletion of your data if there are specific reasons for deletion. This is particularly the case if they are no longer necessary for the purpose for which they were originally collected or processed (Article 17 of the GDPR). You have the right to restrict the processing of your data, which means that your data will not be deleted, but will be labeled in order to limit its further processing or use (Article 18 GDPR). Non have a right to data portability (Article 20 DS-GVO) and a general right of objection (Article 21 DS-GVO).

### **Data Manager:**

Dr. Cornelia Zeidler, OE6860, Department of Hematology, Hemostaseology, Oncology and Stem Cell Transplantation, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hannover.

If you have questions or if you believe that the processing of your personal data is not lawful, you can contact the Data Protection Officer of the Hannover Medical School:

Data Protection Officer of the Hannover Medical School, OE 0007, Carl-Neuberg-Straße 1, 30625 Hannover.

You have the right to complain to the regulator if you believe that the processing of your personal data is unlawful. The address of the supervisory authority responsible for Hannover Medical School is:

The State Commissioner for Data Protection Lower Saxony, Prinzenstraße 5, 30159 Hannover

As part of the data processing, the medical information is encrypted (pseudonymised) before being entered into the database of the SCNIR. If required, re-identification of personal patient data can only be done by the coordinating database center. This may occur if you / your child is desired to decrypt, for example, to obtain a file inspection, or to forward specific information to you or another doctor or clinic. Information about which you can be identified can only be shared with anyone outside our SCNIR after your written consent.

The EMA (European Medicines Agency) requires the respective pharmaceutical manufacturers to report (drug safety study) on the drug safety of drugs used to treat neutropenia, such as filgrastim. For this purpose, anonymized pooled data are evaluated and forwarded in the form of a report.

### **Risks and possible consequences of participation in the SCNIR**

There is no medical risk due to participation in the registry. Any biobank sampling of blood and bone marrow samples (see section on biobank) will generally not require additional blood collection or bone marrow puncture. In most cases it is sufficient that a little more material is taken from a blood or bone marrow control examination than before.

### **Participation in the SCNIR could have the following advantages for you:**

We cannot guarantee that you / your child will benefit directly from participating in this project. However, it may be beneficial to review and review family history and clinical history data, as well as all other clinical findings, by hematology specialists. It may also be beneficial for the SCNIR to know many patients with this condition and to be able to answer their long-term questions and specific risks.

### **Contact**

If you have problems or questions about the SCNIR or your rights as a registered patient, please contact Dr. Cornelia Zeidler; Tel.: 49(0)511-557105, (zeidler.cornelia@mh-hannover.de).

## **Section II: Information on Participation in the Biobank of the International SCNIR**

### **Introduction**

In addition to documenting laboratory and clinical findings in the neutropenia database, the SCNIR collects biological material from registered patients, such as bone marrow and blood smears, as well as cells (bone marrow, blood, skin, and cell extracts, such as DNA and RNA) for the construction of a biobank of the SCNIR, which is located at the University Hospital Tübingen. The material is used for the following studies:

1. When registering, we would like to review the diagnosis using blood count and bone marrow findings. If necessary, this check can be made on the basis of the sent smears.
2. Investigations in the context of research projects whose purpose is to uncover the reasons for the emergence of different forms of neutropenia and their long-term consequences, such as the increased risk for the development of leukemia.

**The additional sample collection is voluntary and only takes place if you give your written consent. Your consent or refusal does not affect the further course of action or further treatment. Participation in the SCNIR biobank is entirely voluntary and independent of participation in the SCNIR.** So you can join the SCNIR without giving your consent to the biobank. As far as you do not want to participate or revoke your consent at a later date, this is possible at any time, there are no disadvantages for you.

Below we will inform you about the objectives of the additional collection of samples, the procedures and the measures taken to protect your personal data so that you can form your own opinion and make a decision on this basis.

### **1. Why are the samples collected?**

The research projects identified causative gene alterations in some of the neutropenic patients in recent years. In addition, genetic markers have been identified that may indicate an increased leukemia risk.

Further investigations are necessary in order to understand the connections between the forms of neutropenia, but also differences, in particular with regard to the long-term consequences and to be able to recognize the characteristics at an early stage.

The goal of this research is not to diagnose you. Rather, biomedical correlations are to be investigated in comparative experiments within a larger, meaningful group of people.

### **2. What kind of biomaterials is it?**

The biomaterial is blood and bone marrow blood, which is obtained in any case as part of routine diagnostics, where a small sample is then taken for research purposes. A separate removal in addition to the anyway necessary material extraction is not provided. If findings

are obtained from the research that made a new sampling desirable, you will be interviewed separately.

### **3. How are the biomaterials used?**

The biomaterials and data provided by you / your child will be used exclusively for the study of severe chronic neutropenia, in particular the causes and sequelae of the disease. **The biomaterials provided may also be genetically engineered, possibly including the entire genetic material (genome).**

**The biomaterials and the data obtained from them should be stored for long term and made available for medical research.** For logistical reasons it is not possible for us to make individual limitations (for example, exclusion of certain research, exclusion of the transfer of biomaterials to third parties). If you do not fully agree with the type and duration of use described, you should not give your consent.

### **4. What are the risks associated with your donation?**

#### **A. Health risks**

The SCNIR asks for your consent to divert a small sample (about 5 ml of heparinized bone marrow and / or 5 to 10 ml of heparinized blood) from the routine check-up and send it to the research laboratory of the SCNIR in Tübingen the storage is sent to the biobank. This removal is therefore not associated with any additional health risk for you / your child. In new cases, however, it may be desirable in individual cases to check the result with additional material - in this case you will be contacted again. The research projects are presented to the patient and the consent for this is also obtained separately.

#### **B. Other risks**

Any collection, storage and transmission of data from you / your child's biological materials as part of a research project will entail confidentiality risks (such as the ability to identify you), particularly with regard to the information about your genetic material. These risks cannot be completely ruled out and will increase as more data is linked, especially if you (for example, genealogy) publish genetic data on the Internet.

### **5. What benefit does it have for you / your child?**

**Personally, you / your child cannot expect any immediate health benefit or benefit from the donation of your samples and data. The results are usually for research purposes only and are not intended to draw conclusions about your health. In individual cases, however, it is possible that a research result could be of considerable importance to your health. This is particularly the case if it results in an urgent suspicion of a serious, previously possibly unrecognized disease that could be treated or prevented from erupting. In such a case, feedback can be sent to you. If you do not want to receive any feedback (right to not know), please delete the possibility of renewed contact in the consent form. You can change this decision at any time by sending us a message. Please note**

that in other places (for example, before taking out a health or life insurance policy) you must disclose information about your health and may suffer disadvantages.

## 6. What benefits does society have?

Medical-scientific research projects aim to improve our understanding of the pathogenesis and diagnosis and, on this basis, to the development of improved treatment approaches aimed at altered cells.

## 7. What happens to your biomaterials and data and how are you protected?

**Information on data protection according to current EU directives:** The legal basis for the processing of your data are Articles 6, 7, 9, 89 of the General Data Protection Regulation in conjunction with §§ 4, 5, 6, 8, 9, 12, 13 of the State Data Protection Act of Baden-Württemberg from 25 May 2018 valid version.

- a. All data directly identifying your person (name, date of birth, address, etc.) will be replaced (pseudonymised) with an identification code immediately after collection of the biomaterials. Thereafter, the record is re-encoded and stored again. Only in this form are the biomaterials and data used for research purposes.
- b. The immediately identifiable data remains in the test site and is stored separately from the biomaterials and medical data. Therefore, samples cannot be returned to you without information from the testing center. An assignment if additional data from your medical records is required to supplement or to re-contact you, if you have given your consent (see 10.). **A transfer of your identifying data to the sponsor, other researchers or other unauthorized third parties, such as insurance agents or employers, does not occur.** Only authorized employees who are bound by professional and data secrecy have access to the pseudonymised database.
- c. To check the correct transfer of treatment data from your medical record into the encrypted study database, authorized persons - so-called monitors or administrators - are allowed to view the personal medical records. These involved employees are also subject to confidentiality. The data collected can also be used or further processed in future research projects of the clinic or institute.
- d. The encoded biomaterials and medical data are kept by the Medical University Hospital Tübingen, but may also be forwarded to research institutes, universities and research companies, and possibly also abroad, for more specific medical research purposes according to previously defined rules. The data may also be linked to medical data in other databases if the legal requirements for this are met. Biomaterials and data released to other sites may only be used for the intended research purpose and not be given to the recipient for other purposes.
- e. The prerequisite for the use of biomaterials and data for a specific medical research project is in principle that the research project has been approved by an independent ethics committee.



- f. Scientific publications are made only in a form in which a conclusion on your person is not possible. The publication of all your genetic information (total genome) is not possible without your express written consent.
- g. With the transfer of the biomaterials to the biobank of the SCNIR, that is the Medical University Hospital Tübingen, they become the property of the Medical University Hospital. You also authorize the SCNIR biobank to use your data collected from the sample collection. The SCNIR biobank uses your biomaterials and data for scientific research purposes only. The samples and data are not sold as such.
- h. You have the right at any time to obtain information about the data concerning you and to correct incorrect data. You can also request that data related to you be deleted at any time. For this please contact the contact mentioned under point 10.

**8. Do you gain a financial benefit from the use of your biomaterials and data?**

You will not receive any compensation for the provision of your biomaterials and data. Should the research be of commercial benefit, you will not be involved.

**9. Will you be contacted again?**

To collect historical data, it may be useful to contact you at a later date and to request additional data or biomaterials from you. In addition, a renewed contact in the context of a feedback of health-relevant results to you in the case of a consent of yours can take place (see under 5.).

**10. What does your right of withdrawal include?**

You may revoke your consent to the use of your biomaterials and data at any time without stating reasons and without adverse consequences for you.

In the case of withdrawal, you can decide whether your biomaterials should be destroyed or used in anonymous form for further scientific purposes. Anonymization means that the identification code is deleted, which can be used to determine the person from whom the sample originates (see point 8a/b above). However, such an anonymization of your biomaterials can never completely rule out the later assignment of the genetic material to your person via other sources.

You can also decide whether your already collected data should be deleted or used in an anonymous form. However, a data erasure can only be made if this is possible with reasonable technical effort. Once the purchase of the biomaterials and the other data on your person has been deleted (anonymization), destruction is no longer possible. In addition, data from analyzes already carried out can no longer be removed.

Please contact for a revocation:

**Prof. Dr. J. Skokowa / Prof. Dr. K. Welte  
Med Clinic II,  
University Hospital Tübingen  
Bettenbau West (501), Eb. 02, Room 532  
Otfried-Müller-Str. 10, 72076 Tübingen**

### **11. Where can I get more information?**

If anything is unclear to you, please ask your doctor or study doctor before giving your consent. If you have any questions, you can also contact the SCNIR biobank at the University Hospital Tübingen at a later date (see address under point 10).