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**Request for approval by the responsible ethics committee for the below described *medical-scientific* project**

(Version 1.0, 24. AUG 2015)

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| 1. Title of the project | Participation in the first medical registry for chronic urticaria, the Chronic Urticaria Registry (CURE) |
| 2. Decisions of other ethic committees | Approval is available from the Ethics Committee of the Charité – Universitätsmedizin Berlin (EA1/146/14) |
| 3. Subject of the registry and its objectives | Chronic Urticaria is one of the most common skin diseases. It is characterized by the recurring appearance of short-lasting, itching wheals, angioedema, or both for at least 6 weeks. Chronic urticaria is subdivided into chronic spontaneous urticaria (CSU) and chronic inducible urticarias (CIndUs), such as symptomatic dermographism, cold urticaria and cholinergic urticaria.  Epidemiological studies were able to demonstrate a point prevalence of 0.5-1% for CSU. For the CIndUs, a lifetime prevalence was shown to be up to 10% for the total population when mild courses are considered.  Publications from past years have demonstrated that many patients with chronic urticaria experience a major impairment of their health-related quality of life (HRQoL). In addition, it has been found that a considerable proportion of patients suffers for years from the disorder.  Despite the high frequency of chronic urticaria and the availability of some retrospectively assessed data on the course of the disease, the epidemiology, duration of disease, course of disease, underlying causes, treatment responses and medical expenses are still insufficiently investigated. While a registry would be an appropriate tool to assess these features, this was, until recently, not available.  For this reason, in the year 2014, the first medical registry for chronic urticaria, the Chronic Urticaria Registry (CURE) was established. CURE is an investigator-initiated, open-ended registry driven by the academic and scientific interests of its participants. CURE is observational (non-interventional) and collects real life data on all types of chronic urticaria patients, suffering from CSU, CIndUs, or both.  Topics of the register include:  1) demographic characteristics of the patients  2) data on the course of disease  3) data on diagnostic measures / underlying causes  4) data on comorbidities  5) data on response to treatment  6) Data on HRQoL  7) data on direct and indirect medical expenses    The aim of the registry is to improve the data for chronic urticaria in the areas mentioned above and, therefore, to improve the understanding of the disease and its subtypes. The results of the medical registry will be published and help to improve care of future patients. |
| 4. Explanation on the intent of the registry. | See section 3. |
| 5. Which of the following regulations shall apply   1. Medical Devices Act 2. Radiation Protection Act 3. X-ray Act 4. Act on Genetic Engineering 5. Data Protection Act | Data Protection Act |
| 6. If applicable: name and characterization of the medical device | Not applicable. |
| 7. Relevant results of pre-clinical test or reasons for not conducting the same. | Not applicable. |
| 8. Content and results of previous projects/applications of the products tested in the registry | Not applicable. No comparable previous studies. |
| 9. Description of the proposed measures/ methods of examination and differences to the usual medical routine (what is „routine“, what will be done differently because of the registry?) | This registry will not affect the management and treatment of the included patients. It is a pure observational (non-interventional) registry. Accordingly, the patients will not be treated differently with regard to the usual medical routine. Only the entry of patient data into the registry is different in these patients. In addition, validated patient reported outcome instruments, such as quality of life questionnaires, will be handed out to the registry participants that may not be part of routine care. In this context, it is important to stress that no personal data such as name, initials, date of birth, address, are recorded in the registry. The entered data will be pseudonymized so that only the entering physician knows which actual patient belongs to which registry record. The recording physicians are asked to put a note in the original patient chart, documenting that the patient is in the registry.  Prerequisite for adding a patient to the CURE is that the patients are informed thoroughly about the aims and nature of the registry with the patient information form and that a dated and signed written informed consent is obtained from the patient.  One aim of the registry is to obtain better data on the course of chronic urticaria. Accordingly, a basic entry of the patient’s data will be followed by follow up entries (around every 6 months).  The chronic urticaria registry should gather data from chronic urticaria patients from all over Germany, Spain, France, Italy and the UK (core countries). However, the registry should also be extended to additional countries, including North America and Asia.  Below the most important steps of the establishment of the CURE are listed:  1) In a first step, an International Steering Committee (ISC) for the CURE was convened. The main tasks of the ISC are to develop the specific questions of the CURE, to decide on specific data analyses of CURE data and to supervise the latter as well as to decide on adjustments/updates of the registry content. Members of the ISC consist of one representative for each participating core country as well as the coordinating principal investigator of the registry. The ISC-members also serve as a main contact person for the CURE in their country. Currently the ISC consist of the following members:  Marcus Maurer  Dept. of Dermatology and Allergy  Charité – Universitätsmedizin Berlin  Germany  Karsten Weller  Dept. of Dermatology and Allergy  Charité – Universitätsmedizin Berlin  Germany  Ana Maria Gimenez-Arnau  Department of Dermatology  Hospital del Mar. IMAS  Universitat Autonoma Barcelona  Spain  Pascale Mathelier-Fusade  Centre d’Allergologie  Hópital Tenon, Paris  France  Riccardo Asero  Ambulatorio di Allergologia  Clinica San Carlo, Milan  Italy  Clive Grattan  Dermatology Centre  Norfolk and Norwich University Hospital  UK  2) In a second step, the actual web-based registry was programmed. To this end, the CURE questions were entered and implemented in a well-established eCRF program with audit trail, the backbone of the CURE. The name of the eCRF system is secuTrial, a FDA/GCP compliant software.  3) In a third step, the registry was first activated for the entering center at the Dept. of Dermatology, Charité – Universitätsmedizin Berlin, after approval of the responsible ethics committee and the data protection officer was available.  4) The next steps consists of the involvement and activation of additional entering centers and entering physicians into the CURE registry. Moreover, a patient module will be set up in the future in order to obtain direct input from the affected patients, mainly based on already well-established patient reported outcome (PRO) tools. |
| 10. Evaluation and assessment of the foreseeable risks and disadvantages linked to a registry participation compared with the expected benefits for the participants and future affected individuals (benefit-risk-estimation). | Registry participation is not linked to any risk or disadvantage for the patients. The same applies to a refusal of participation. |
| a. Foreseeable therapeutic benefit for the registry participant (**individual benefit**) | Not applicable. |
| b. Foreseeable medical benefits for future affected individuals **(group benefit)** | New insights into chronic urticaria, its course, causes, comorbidities, treatment response and impact can be expected from the results of the CURE. This will help to improve the understanding of the disease and may also serve to improve the future care for chronic urticaria affected individuals. |
| c. **Risks** forand burdens on the registry participants | None. |
| 11. Measures of risk control | Not applicable. |
| 12. Criteria for termination | Not applicable. |
| 13. Number, age and gender of the persons concerned | All patients affected with chronic urticaria for whom a dated and signed written informed consent is available can be recorded in the registry. There is no limit with regard to the number, age or gender of the patients. No selection of patients is intended since it is the aim to collect unbiased data from the real life clinical setting. |
| 14. Statistical planning and specification as well as biometric justification of the number of cases and signature of the involved statistician | Not applicable. It is neither intended to have a time limit of the registry, nor a limit regarding the number of enrolled persons. |
| 15.  a. List of and, if applicable, explanation of the **in- and exclusion criteria** | All affected patients with CSU, CIndUs, or both can be enrolled/recorded in the registry if a written, dated and signed informed consent is available. |
| b. **Patient information** (who informs the patients and how; how much time is intended between the information of the patients and the patient’s consent; a reference to the content of an attached patient information is possible) | Prerequisite for adding eligible patients to the CURE is that the patients are informed thoroughly about the aims and nature of the registry with the help of the available patient information form (please also see attached form) and that a dated and signed written informed consent is obtained from the patient. Potential patients will have sufficient time to decide for or to decide against an entry to their data into the CURE. |
| c. **Informed Consent** (a reference to the content of an attached informed consent form is possible) | See attached written informed consent form. |
| d. If applicable: **information and consent of the legal representative** | Given that the patient concerned may not be of legal age, or if there is a guardianship in place, patients as well as parents or guardians will be informed about the registry. Before including patient data into the registry, a dated and signed written informed consent of the person concerned or the parent / guardian (i.e. the legal representative) must be available. |
| 16. Procedures for the recruitment of participants to the registry | A recruitment of patients will be done out of the normal, routine clinical care situation. |
| 17. If applicable: **Reason for the inclusion of patients who are underage and / or are not able to provide an informed consent.** | The data for the CURE should be collected from the real life treatment situation in clinical practice (observational approach). As children and adolescents (minors) can also be affected by chronic urticaria, it makes sense to not exclude these patient groups from participation.  Patients for whom it is not able to obtain a dated and signed written informed consent will not be included in the CURE. |
| 18. Relationship between participants and investigators/entering physicians (Is the investigator / entering physician at the same time the treating physician?) | In is highly probable that the patient data entering physician/investigator and the treating physician caring of the respective patient are identical in most cases. |
| 19. Statement regarding the inclusion of possible dependents of the investigator / entering physician or the sponsor. | Dependents of the investigator / entering physician or the sponsor are not included in the registry. |
| 20. Procedures that allow a determination whether a participant of the registry takes part in a clinical study at the same time or whether a participant is still in a pre-specified post participation time period of a clinical study. | This is a pure observational (non-interventional) registry that cannot be influenced by clinical studies and that does not influence clinical studies. Accordingly, there are no intended measures to determine whether a participant of the CURE takes part in a clinical study at the same time or whether a participant of the CURE is still in a pre-specified post participation time period of a clinical study. |
| 21. If applicable: honorarium or reimbursement for registry participants | None. |
| 22. If applicable: Plan for further treatment and medical care of the participating patients after the end of the registry | Not applicable. |
| 23. If applicable: insurance for the participants | Not applicable. |
| 24. If applicable: procedure of registry documentation | All relevant CURE data will be abstracted from the patient charts and entered into the CURE eCRF. The name of the eCRF system is secuTrial, a FDA/GCP compliant software. The data abstracted from the patient record may be adjusted/changed over time (in case these changes are decided and approved by the International Steering Committee of CURE). |
| 25. If applicable: description how the medical condition of healthy participants should be documented. | Not applicable. |
| 26. If applicable: methods to determine adverse events as well as to document and to report the latter | Not applicable. |
| 27. Procedures in order to protect the confidentiality of the obtained and stored data, documents and, if applicable, samples. Description of the encoding of registry participants data (*please no use of initials and date of birth for the encoding!)* | All patient data will be entered [pseudonymized](https://www.dict.cc/englisch-deutsch/pseudonymised.html) into the eCRF of the CURE. Personal data (name, initials, date of birth, address, etc.) will not be entered into the registry.  The basis for the later data processing and analyses of the registry data will solely be the data available in the CURE eCRF.  The CURE eCRF is protected by a secure login, The name of the eCRF system is secuTrial, a FDA/GCP compliant software. |
| 28. Statement regarding the compliance with data protection | All relevant data protection regulations will be adhered to within the urticaria registry. |
| 29. Names and addresses of institutions that are involved as registry center or registry laboratory in the registry as well as of the principal investigator and investigators / entering physicians of the registry. | Registry centers:  Dept. of Dermatology and Allergy  Charité – Universtiätsmedizin Berlin  Charitéplatz 1  10117 Berlin  Germany  Project manager:  PD Dr. med. Karsten Weller  In addition, other centers / urticaria patient treating physicians in Germany, France, the UK, Italy, Spain and other European and Non-European countries will enter data to the registry.  Since this is a non-interventional project no specific registry laboratory exists. |
| 30. Details regarding the qualification of the registry center, particularly regarding the sufficiency of the existing resources and personnel (and its experience in the conduct of similar studies) | The center has experience with clinical trials. Adequate resources and personnel exist in order to take part in the CURE. |
| 31. Statement regarding the access of the entering physicians/investigators/principal investigator to the registry data and regarding the publication policy | Every entering physician / investigator has access to his own entered data.  It is intended to publish CURE data results in scientific journals. The data from the CURE are planned to be analyzed twice yearly. The International Steering Committee (ISC) will discuss and decide on possible CURE publications. The scientific neutrality of publications arising from the CURE cannot be restricted in any way. |
| 32. Details on the financial funding of the registry | The registry is partially financed by:    Urticaria Network e.V. (UNEV)  Charitéplatz 1,  10117 Berlin  European Academy of Dermatology and Venereology (EADV)  via S. Balestra 22B  CH-6900 Lugano  Switzerland  In addition, the acquisition of funding from various other sources is planned. This includes the European Academy of Allergy and Clinical Immunology (EACCI), the WAO (World Allergy Organization) and as well pharmaceutical companies and other stakeholders. |
| a. Source of funding (name and main office) | Urticaria Network e.V. (UNEV)  Charitéplatz 1,  10117 Berlin  European Academy of Dermatology and Venereology (EADV)  via S. Balestra 22B  CH-6900 Lugano  Switzerland |
| b. Amount of calculated costs per participant and in total | A cost calculation per participant is not possible due to the nature of this registry.  In total, the costs for establishing and hosting the urticaria registry in the first three years (2014, 2015, 2016) are currently estimated to be around 100.000 Euro. However, depending on the speed of expansion, success, promotion and available financial funding of the registry, the costs may also become considerably higher. |
| c. Amount of reimbursement per participant and in total | There is no reimbursement intended for patients included in this registry. |

I hereby certify that the information provided in this application is correct. I believe that it is possible to perform the above mentioned patient registry in accordance with the project plan and the national legislation.

Last Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

First Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Address: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Position: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date: \_\_\_\_\_\_\_\_\_\_\_\_\_ Signature of the applicant: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_