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| START DATE: | 01/02/2018 |
| END DATE:   | 31/01/2021 |
| DURATION:   | 36 month(s) |
| CURRENT STATUS: | Ongoing |
| PROGRAMME TITLE: | 3rd Health Programme (2014-2020) |
| PROGRAMME PRIORITY: | - |
| CALL: | Rare diseases - support for New Registries |
| TOPIC: | Rare Disease Registries |
| EC CONTRIBUTION: | 398138.23 EUR |
| KEYWORDS: | Core Dataset, E-Hod, E-Imd, Ema, Erknet, Hpo, Inherited Metabolic Diseases, Intd, Metabern, Orphan Drugs, Pass, Patient Perspective, Phenotyping, Post-Authorization Surveillance, Registry |
Project abstract

More than 700 inherited metabolic diseases (IMDs) have been identified so far. Each single IMD is a rare condition, but collectively IMDs are affecting at least one in 500 newborns. Clinical presentation of IMDs is wide-ranging from involvement of single organ systems to multi-systemic disease, confronting patients with significant and often severe health problems resulting in high morbidity, reduced life expectancy, and low quality of life.

For a limited number of IMDs networking activities already exist on a European or international level. The E-IMD, E-HOD and iNTD family of IMD registries has a relevant impact on improving the health of patients with IMDs and facilitates post-authorisation safety studies (PASS) for orphan drugs. However existing registries still do exclude a significant portion of IMDs and do not fulfill all core recommendations made by the European Union Committee of Experts on Rare Diseases (EUCERD). The recent inception of the European Reference Network for Hereditary Metabolic Diseases (MetabERN) lays the foundation for the development of an overarching European IT platform for IMD registries.

The project consists of 3 components: (1) a novel registry platform for all known IMDs, (2) an upgrade of existing IMD registries and (3) a collaboration with the European Rare Kidney Disease Reference Network (ERKNet). The new Unified European Registry for Inherited Metabolic Diseases (U-IMD) will encompass all known IMDs, fully implementing EUCERD recommendations.

Data modules developed for U-IMD will be integrated in the existing IMD registries, with the iNTD registry as pilot, thus reaching interoperability of patient records. MetabERN and ERKNet will develop a common standard for minimal core data sets.

The U-IMD registry will follow an open multiple stakeholder approach, explicitly seeking collaborations with national and EU level health authorities, other scientific networks and consortia, patient and parent organizations and industry.
Work package

Work Package 1: Coordination of the project
Start month: 1
End month: 36
Work Package Leader: UKL-HD

All main management tasks will be carried out by UKL-HD, closely supported by the co-applicants HSJD, OPBG, VFN v Praze and HSK-WI in their function as iNTD, E-IMD and MetabERN network representatives and by the collaborating stakeholder E-HOD represented by Henk Blom.

T1.1. Executing management tasks: Carrying out overall management activities in close collaboration with the other work package leaders.
T1.2 Ensuring common work commitment: Establishing an internal partnership agreement.
T1.3. Communication management: Undertaking all possible measures for facilitating efficient communication processes within the project, guaranteeing a high standard on knowledge on project activities among all collaborators.
T1.4. Financial management: Taking on responsibility for all financial issues. All financial beneficiaries in the project will be obliged to provide cost statements in due time.
T1.5. Coordination, controlling and monitoring: Coordinating all project activities, creating transparency, accountability and early awareness for challenges and opportunities in the workflow. Organising steering group meetings every three months and on demand by holding telephone or video conferences and at least once a year in person, harmonized with the other annual registry meetings preferably during the Society of the Study of Inborn Errors of Metabolism (SSIEM; http://www.ssiem.org/home/welcome.asp) conference. At each meeting Work Package Leaders are expected to report upon new developments, progress, opportunities, challenges and obstacles encountered during their operational work, with special regards to timely achievement of milestones and deliverables.
T1.6. Ensuring good clinical practice: Monitoring registry activities with regard to protection of personal data, obtaining of IRB vote and informed consent according to local requirements and implementation of SOPs.
T1.7. Stakeholder liaison: Managing all stakeholder liaison activities with interested parties including other research networks, professional societies, patient and parent organisations, policy makers and industry.
T1.8 Sustainability: Devising and implementing a strategy for long term sustainability of registry and network activities.

Work Package 2: Dissemination of the project
Start month: 1
End month: 36
Work Package Leader: VFN v Praze
All main tasks of dissemination will be carried out by VFN v Praze closely supported by the co-applicants HSK-WI, UKL-HD, HSJD and OPBG and the collaborating stakeholder E-HOD represented by Henk Blom, with special focus on providing work products to be disseminated, opportunities for dissemination and support as network representatives.

T2.1 General dissemination: Creating awareness for existence and proceedings of the project among stakeholders by establishing a project website and creating and distributing a promotional leaflet. The website will serve as a platform to provide stakeholders with brochures, newsletters, meeting announcements and new publications. Project related information for patients and their families will be written in English and translated into the patient’s own language.

T2.2 Targeted dissemination: Specific communication to professionals and stakeholders with a high multiplier effect like patient organisation and research networks or societies by presenting scientific findings and project results at relevant meetings and well-established conferences and congresses.

T2.3 Patient and parent involvement: Facilitating the capturing of patient and parent perspectives by motivating participation in the registry and usage of registry tools at patient and parent group meetings.

Work Package 3: Evaluation of the project
Start month: 1
End month: 36
Work Package Leader: OPBG

All main tasks of Evaluation will be carried out by OPBG closely supported by the patient advocacy groups BOKS, the Belgian Patient Organization for Rare Metabolic Diseases (represented by Lut de Baere) and Gaucher Association UK (represented by Tanya Collin) as collaborating stakeholders.

T3.1 Evaluation plan: Setting up an evaluation plan considering the targets of the specific objectives.

T3.2 Evaluation group: Forming an evaluation group composed of key collaborating stakeholders and coordinating annual meetings harmonized with the annual meetings of the steering group.

T3.3 Evaluation of data collected in the registry: Analysing data in the registry with regard to geographical coverage, coverage of the MetabERN disease panel and quality and completeness of records.

T3.4 Evaluation of mode of data collection: Checking project progress against defined milestones, stated project aims and recommendations developed by EUCERD.

T3.5 Monitoring: Working in close collaboration with the coordination work package, pointing out opportunities and challenges identified during evaluation.

T3.6 Reporting: Managing the process of preparing the evaluation report.
Work Package 4: Patient Registry

Start month: 1
End month: 36
Work Package Leader: UKL-HD

Main tasks will be carried out by UKL-HD with support and close involvement of the co-applicants HSJD, OPBG, VFN v Praze and the collaborating stakeholder MetabERN represented by Maurizio Scarpa and E-HOD represented by Henk Blom and ERKNet represented by Franz Schaefer.
Designing the data model to be employed by U-IMD is a special focus of work for all applicants and collaborating stakeholders alike and will be initiated and coordinated by UKL-HD. In their roles of network representatives HSJD, OPBG, MetabERN and E-HOD will additionally work on activating the respective networks for reaching sufficient numbers of metabolic expert-centres actively using U-IMD and thus attaining adequate patient numbers in the registry. UKL-HD will carry the main workload of technical implementation and upkeep of the registry and support data entry of all project partners.

T4.1 State of play: Assessing structures and recommendations developed by other rare disease registry projects, designing the U-IMD data model.

T4.2 Patient registry: Programming of a web-based password-protected registry suitable for all known inherited metabolic diseases and for individuals with suspected IMDs but yet unknown molecular origin, mapping onto the data models of existing registries and introducing controlled and standardized vocabularies for recording phenotypic clinical abnormalities and drug treatment, as well as tools for capturing the patient perspective.

T4.3 Interoperability: Making the existing iNTD registry interoperable with the new registry.

T4.4 Registry administration: Managing the operational work of the registry, including assurance of data quality, user support, user training, data extraction and data processing.

T4.5 Data entry: Registering of patients and data entry by clinical partners who are experts in the field, following local legal requirements, obtaining informed consent and ascertaining cases prior to registration.

T4.6 Data analysis: Analysis of data collected in the registry and facilitating the work of other work packages by providing descriptive data and analysed data.
COORDINATOR

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<table>
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<th><strong>OUTPUTS</strong></th>
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| **Layman version of the final report**  
VFN v Praze  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
This is a short (e.g. 10 pages) version of the final report, written for the interested public as a target group. |
| **Layman version of the final report**  
VFN v Praze  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
This is a short (e.g. 10 pages) version of the final report, written for the interested public as a target group. |
| **Patient registry**  
UKL-HD  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2019  
The U-IMD patient registry as specified in the project plan is accessible and supported throughout the project. |
| **Minutes of annual meeting 2**  
UKL-HD  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/05/2020  
Work Package Leaders report upon new developments, progress, opportunities, challenges and obstacles encountered during their operational work, with special regards to timely achievement of milestones and deliverables. |
| **Minutes of annual meeting 3**  
UKL-HD  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
Work Package Leaders report upon new developments, progress, |
opportunities, challenges and obstacles encountered during their operational work, with special regards to timely achievement of milestones and deliverables.

**Annual meeting 3**  
**UKL-HD**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
Work Package Leaders report upon new developments, progress, opportunities, challenges and obstacles encountered during their operational work, with special regards to timely achievement of milestones and deliverables.

**Evaluation report**  
**OPBG**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
This report evaluates all project activities one the achievement of the specific project aims and thus on the contribution to further the general objective.

**Interoperability of U-IMD and iNTD**  
**UKL-HD**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/08/2019  
Interoperability of iNTD and U-IMD patient records is achieved.

**Evaluation report**  
**OPBG**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
This report evaluates all project activities one the achievement of the specific project aims and thus on the contribution to further the general objective.

**Interim report(s)**  
**UKL-HD**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/08/2019  
This report describes the activities carried out, milestones and results achieved.
in the first half of the project. Deliverables can be attached as annexes.

**Final report**  
**UKL-HD**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2021  
This report describes the project implementation and the results achieved. The deliverables are annexed.

**Leaflet**  
**VFN v Praze**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/05/2018  
A leaflet to promote the project must be produced at the beginning.

**Report on the analysis of data collected in the registry**  
**UKL-HD**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/11/2020  
Analysis of data collected in the registry and facilitating the work of other work packages by providing descriptive data and analysed data.

**Web-site**  
**VFN v Praze**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/05/2018  
Each project must have a dedicated web-site / web-pages. This can have a public part and another one accessible only to the applicants.

**Report on the evaluation plan**  
**OPBG**  
Unified European Registry for Inherited Metabolic Disorders (U-IMD)  
Expected on: 01/02/2020  
This report evaluates the setting up of an evaluation plan considering the targets of the specific objectives.
Report on the evaluation of data collected in the registry
OPBG
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Expected on: 01/11/2020
This report refers to the evaluation of the data collected in the registry (geographical coverage, coverage of disease panel, quality, completeness.

Report on the evaluation of mode of data collection
OPBG
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Expected on: 01/11/2020
This report evaluates the mode of data collection (Checking project progress against defined milestones, stated project aims and recommendations developed by EUCERD)

Interoperability of UIMD and iNTD
UKL-HD
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 27/09/2019
Report on the Interoperability of U-IMD and iNTD

Minutes of annual meeting 1
UKL-HD
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 15/05/2019
Work Package Leaders report upon new developments, progress, opportunities, challenges and obstacles encountered during their operational work, with special regards to timely achievement of milestones and deliverables.

Patient registry
UKL-HD
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 11/04/2019
Description of the Content of the already established Patient registry

Justification related to the level of dissemination: This deliverable should stay confidential because the patient registry will contain patient data. According to the data protection laws of all participating countries patient data must always stay confidential. Besides the study central in Heidelberg and the treating physician and it’s team no one should have access to the data in the registry.

User manual for data entry
UKL-HD
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 11/04/2019
A user manual to facilitate the data collection and entry into registry.

Report on the development of a minimal core data sets
UKL-HD
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 11/04/2019
This report evaluates the development of a minimal core data set to be shared with the upgraded ERKNet registry.

Web-site
VFN v Praze
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 30/05/2018
Each project must have a dedicated web-site / web-pages. This can have a public part and another one accessible only to the applicants.

Leaflet
VFN v Praze
Unified European Registry for Inherited Metabolic Disorders (U-IMD)
Published on: 03/04/2018
A leaflet to promote the project must be produced at the beginning