TOOL 7

Case Studies for Public-Private-Collaborations in the Rare Disease Space

Together4RD
RARE DISEASES

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Together4RD Toolkit to foster ERN and Industry Collaborations

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Introduction

As part of the significant preparatory work leading up to the submission for publication of the Together4RD Position Statement, Together4RD sought examples of ongoing or past public private partnerships in the rare and highly specialised healthcare field. The reason for this information gathering was three-fold:

- ☑ To ameliorate any concerns within the ERN Board of Member States (BoMS) about public private partnerships in this field
- ☑ To collect learnings on the set-up and delivery of the activities involved.
- ☑ To inspire ERNs and Industry (especially in less research-mature fields) as to the kind of activity ERNs might enter into with Companies

These case studies tended to fall into two categories – registry-connected, or else concerned with advancing clinical research broadly, outside of clinical trials specifically. They were presented in brief as part of the supplementary material for the **Together For Rare Diseases Position Statement**.

TREAT-NMD

This case study highlights the achievements of a specific community, namely the neuromuscular field, in establishing both registry-related and broader clinical research activities involving partnerships with Industry.

TREAT-NMD was established back in 2007 as a European 'Network of Excellence', via an FP6 grant, in order to advance trial-readiness in all neuromuscular diseases. **It has played a key role in bringing together the right experts - patients, advocacy organisations, healthcare professionals, researchers, AND pharmaceutical organisations – to drive progress**. It has created a suite of tools and activities to achieve its goals, and in 2019 was 'spun out' of Newcastle University (the original grant holder and thus Network coordinator), as its own legal entity. Many key resources were established under that initial grant, to help extend translational research, these include:

- cell and animal standard operating protocols (for preclinical research);
- a unique advice service, TACT (**the TREAT-NMD Advisory Committee for Therapeutics**)
- global patient registries
- care guidelines, and family guides
- and more

From the early stages of TREAT-NMD, **Industry has always been acknowledged as a key stakeholder and driver of treatment development.** In the original project phase, companies were included as members of the consortium, to ensure the tools developed during the grant funded period actually met the needs of industry. Consequently, many of the activities and outputs listed above involved close public-private collaboration, and ethically-robust practices and codes have been developed to facilitate this.

One key area of TREAT-NMD Industry engagement concerns patient registries, to improve understanding of disease, help build trial-ready patient cohorts, and boost patient recruitment. TREAT- NMD created tools and approaches to connect numerous autonomous registries for the more common neuromuscular diseases (NMDs) NMDs like DMD and SMA. To create greater interoperability and increase the power of standalone registries for these conditions, TREAT-NMD developed both core and expanded datasets to standardise data. At the same time, TREAT-NMD coordinated the creation of global patient registries for rarer NMDs, for which one single registry worldwide makes better sense. The result of all this work

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is a network of inter-connected registries able to provide a wealth of information, which can be queried by academic sites (for free) or by Companies (for a fee). Industry have purchased anonymised data of this sort for many years, which supports feasibility studies or enables patient recruitment in clinical trials. The model established back in the days when TREAT-NMD was coordinated by Newcastle University saw those funds from Companies invested back into the core staff involved in running the network, and/or to support networking of the registries themselves. Now that neuromuscular therapies are approved, TREAT-NMD Services Ltd (a dedicated legal entity which spun out of Newcastle University in 2019) is expanding the registries to be able to carry out Post Marketing Surveillance on a global scale.

These days, there are 65 registries collaborating with TREAT-NMD as the 'TREAT-NMD Global Registry Network (either for NMD generally or for a specific condition) and they together collect data on approximately 88,800 people living with an NMD. Many of the processes initially established under the days of the TREAT-NMD network remain in place, to support Industry interactions. **One major form of interaction with Industry concerns access to registry data**. When a Company wishes to purchase data from the global registries, for instance to perform a feasibility assessment, the requests are considered by a committee set-up very early on in the TREAT-NMD lifetime – the is the TGDOC or TREAT-NMD Global Registries and Data Oversight Committee. It has been very important to TREAT-NMD, both as an initial Network of Excellence funded by the EU, and now as a ltd company, as well as its 'in-between' stages, to ensure Industry interaction around accessing registry data is appropriate and handled robustly, recognising the key importance of this stakeholder group but also acknowledging the need for the highest ethical approaches. Tools have been developed to support this, and build transparency, such as the **TGDOC Charter**. **However, the engagement has been far more substantial than individual Companies simply purchasing data (whether as a one-off or on a longitudinal basis). Crucially, TREAT-NMD has always partnered, and continues to partner, with Industry on all activities**, as appropriate, to ensure the end products and outputs will be useful to Industry – and this is very much the case with the registry-related activity. For instance, Industry experts are always consulted when core and expanded datasets are being developed or updated for the individual conditions, to ensure the needs of Companies are reflected in the type of data being collected, and that the way in which the data is being collected is standardised and appropriate.

Beyond the registry-related activities, TREAT-NMD engaged with Industry to advance clinical research via other means. One important tool developed by the initial Network of Excellence is the CTSR (care and trial site registry), which was designed to provide information on personnel facilities, patient populations, and prior experience with conducting clinical trials. Sponsors can use the resource to help select experienced trial sites, and provided input to its original creation.

Another key resource -which is perhaps more in the category of 'Industry as a customer' rather than a co-creator- is the TREAT-NMD Advisory Committee for Therapeutics (TACT), which allows a better prioritisation of compounds to be taken from preclinical studies into clinical trials. TACT was established in 2009 to de-risk trials and ensure compounds moving into clinical trials have the best possible chance of making it to patients. Anyone can apply for a TACT review, and the goal is to help the applicant – commercial or otherwise- to position a candidate therapy along a realistic and well-informed pathway to clinical trial and eventual registration, by identifying potential pitfalls in the translational process and by providing transparent advice. Each application is given a bespoke international expert panel made up of preclinical, clinical, regulatory, patients and industry experts. Where the application is a Company, there is a fee for this advice and the report which follows an in-depth real-time review meeting. The way the model was set-up under the TREAT-NMD network saw all funds raised in this way being used to support the core running of TACT. Naturally, a high level of confidentiality is maintained.

Other TREAT-NMD interactions have included Industry funding training events, summer-schools and educational webinars (without playing a direct role in setting agendas).

In terms of the mechanisms of governance for Industry interactions – in the original grant, everything was covered by confidentiality agreements within the project consortium. Outside of this, and in the years since that grant came to a close, bespoke contracts and agreements have been set in place, such as the TGDOC Charter to govern the registry enquiries, as above, CDAs (Confidential Disclosure Agreements) and other contracts. The way in which contracting has worked has changed over the years. These days, TREAT-NMD is a not-for-profit organisation and its own legal entity, and so can undertake contracting directly with any given Company. For many years, however, when the TREAT- NMD Network was NOT a legal entity, contracting was performed by and centred around Newcastle University, as the representative of all the other entities involved in the network. This was not ideal, in some ways, as it meant the University legal department had to be brought on board and learn how to do this kind of work, which is not always obvious (especially in risk-averse organisations). Some of the processes involved in contracting and handling funding, for instance, were more bureaucratic than the experts involved would have liked. This was one of the reasons, in the end, that TREAT-NMD became a spin-out. However, the key point is that a great deal of collaboration *was* possible through this model of a non-legal-entity network, with one party (which *was* a legal entity) acting on behalf of the rest.

In summary, TREAT-NMD has been very influential in advancing clinical research in the NMD field. Considering the activities and collaborations with Industry summarised above, an important ingredient for success was building a truly multistakeholder network and community from the start, which entailed recognising the value of Industry as a stakeholder, even in the early days. The approach was very much to develop any and all tools which would have a relevance to Industry, WITH Industry, and also ensuring an international and global approach.

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The Sanofi Genzyme French Pompe Registry

This is an example of a national registry for a particular condition, established by Industry as part of a multistakeholder collaboration.

The main treatment for Pompe Disease is enzyme replacement therapy (ERT), and Sanofi provides two ERT products – Myozyme, approved almost 20 years ago, and Nexviazyme. This national registry was first qualified by the French National Committee for Rare Diseases Registries (CNR-MR) supported by INSERM and institut national de veille sanitaire (InVS), in 2008, to collect prospective clinical, functional and biological data on all French patients with a Pompe disease diagnosis (whether treated or not). The different stakeholders first discussed need and goals for the registry, and, after agreeing a plan, Sanofi established contracts with a group of French hospitals (individual contracts with each), to obtain consent from patients and provide the data. These contracts are updated on a one-to-one basis, as needed. Funding is provided by Sanofi to the research teams of the hospital, to support the data entry, but is also supplemented with funding from the French Association against Myopathy (AFM), French Glycogenosis Association (AFG), INSERM, and InVS. The registry serves multiple purposes:

- Elucidates the natural history of Pompe disease
- Enables the medical community to develop patient monitoring recommendations
- Optimises patient care
- Enables an assessment of the long-term effectiveness of the ERT

The results of the Registry data collection are published annually. Details of the registry dataset and patients enrolled are **available here**.

Key to success here was the fact that both main parties (the hospitals and Sanofi Genzyme) were 'on the same page' and saw value in the proposal. In terms of challenges, the need to contract with each hospital can be time-consuming. Furthermore, when regulators request data from the Company, regarding the ERT, it is the individual clinicians who are actually having to provide the data – in other words, the data access process could be improved.

ERK-REG

This case study is an example of how one of the registries created by the ERNs, for rare renal conditions, has interacted with Industry in its early years.

ERK-REG is the registry of the ERKNet ERN, for rare renal diseases. It was initiated in 2019 and acts as a single core registry for all rare renal diseases. The Registry collects data from the HCPs which are part of the ERN and is able to serve multiple purposes:

- Epidemiology of rare kidney diseases Information on level of diagnostic ascertainment (inc. access to genetic testing)
- Phenotype and natural history information
- Continuous monitoring of diagnostic and therapeutic performance and guideline adherence for optimized patient outcomes
- Rapid identification of patient cohorts for clinical trials

Early collaborations with Industry (i.e. prior to the Together4RD pilots) included ERK-REG brokering contracts between an Industry sponsor and sites that have patients eligible for clinical trials. Another example involved contracting with large pharma to provide aggregate data on over 200 paediatric patients receiving a medicine off-label (which was used as supportive evidence for a Paediatric Investigation Plan). There is an aspiration to use fully anonymized patient-level registry data to create external control arms for clinical trial, in future.

By 31st December 2023 a total of 22,687 patient records had been included in the ERK-REG (8928 by adult units (39,4 %), 13,758 by pediatric units (60,6 %), across 53 ERKNet Member centres, 5 Affiliated Partner centres, and 42 other external centres - **see here**.

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European Society for Bone and Marrow Transplantation Registry (EBMT)

This case study involves Industry accessing a key registry established by a non-profit society, and using that data for a range of regulatory purposes.

The EBMT (European Society for Bone and Marrow Transplantation) is a non-profit Society founded in 1974. Originally, the scope was purely clinical bone marrow transplantation, but more recently, cellular therapies have also been included. It is a collaborative network for professionals working in centres and individuals in field of HSCT, gene and cell therapy – it has over 5000 members in over 70 countries, including over 600 transplant centres (covering >90% of all transplant centres in Europe).

The three pillars of the EBMT are research, education, and patient care. The EBMT Registry is the backbone of EBMT's research and educational activities. It contains patient clinical data, including aspects of the diagnosis and disease, first-line treatments, haematopoietic stem cell transplant (HSCT) or cell-therapy-associated procedures, transplant type, donor type, stem cell source, complications, and outcomes.

EBMT provides data to its members (ranging from individual physicians and nurses to Centres) and is able to perform studies and assess epidemiological trends. Industry are long-time collaborators in the EMBT broadly. Companies can become partners of excellence, without voting rights. If they wish to participate in one of the EBMT scientific studies, using the Registry, they negotiate payment. Of particular note is the success in gaining EMA qualification (specifically of the cell therapy module): to- date, EBMT has made various agreements with Companies on a one-to-one basis to support their Post Authorisation Safety Studies, based on secondary use of the Registry data. At present, no direct access is provided to the Registry data - rather, Companies approved as partners of excellence can access data collected in reports. In addition, Companies can contract for individual research projects, such as feasibility reports, surveys, conducting retrospective or prospective studies, etc. Where possible, only anonymous data is shared (although pseudonymised data can be shared with explicit patient consent). The Registry facilitates over 100 publications per year.

https://www.ebmt.org/ebmt-patient-registry

French Proof of Concept Club (POC Club)

This is an example of a national (French) initiative to promote more rare disease research collaborations between the public and private fields

The POC Club is a national (French) resource to promote innovative research and develop new treatments for rare diseases by offering coaching and guidance for researchers and clinicians and, crucially, connecting them with suitable Industry partners. Established in 2017, it is recognised in the 3 rd French National Plan for Rare Disease. POC is essentially an effective business model, based on a research valorisation tool & implemented through a group of industry partners. The initiator for the idea was the Foundation Maladies Rares, and the goal was to bridge the gap between academia and industry in rare disease. POC Club is financed through company partners and wider fundraising. Webinars allow academics to present 10 minute 'elevator-pitches' for projects they wish to conduct, and the Industry feasibility of the research proposals is assessed. They run two sessions per year – over the first 5 years, 85 projects have been presented to Industry through the POC Club, with 70 connections made, and an 80% interest rate from the Industry participants. If a project is taken forward by a Company, partnership agreements can be signed between the key actors and a tech transfer office.

The first success of the POC was the creation of a **partnership** (signed in April 2018) between industry, an academic researcher, and a Tech-Transfer Office, to develop a gene therapy for Fragile X Syndrome.

This partnership led to an Exclusive Worldwide License Agreement in 2021. Factors for success in this arrangement included:

- The stakeholders coming together at an early stage in the research
- Each partner contributing with their unique experience and capabilities, and valuing what the other could bring
- An understanding of the expectations and constraints of the other partner
- A neutral and trusted third party to initiate and facilitate the partnership

The POC Club has encountered several challenges in attempting to establish collaborative projects between academic researchers and Industry. For instance, there are different expectations from Industry depending on the size of the company – large pharma companies have different needs, perspectives and expectations to small biotech companies. The gap between academia and industry is very much real, and has to be addressed. In particular, academic researchers are not aware of the expectations and constraints Industry has to deal with. It has proven very important, therefore, to coach researchers and clinicians to better understand the key milestones of drug development. POC Club plays an important role by acting as a third party to facilitate the discussions and help move things forward (**especially when addressing IP matters**).

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Innovative Therapies for Children with Cancer (ITTC) Consortium

This is a well-established case study from the paediatric cancer community, dating back over 20 years, in which Industry is a long-term collaborator in efforts to improve the whole lifecycle of product development in paediatric oncology.

The Consortium involves 63 Paediatric Oncology Departments in 18 European countries with expertise in conducting early phase trials in children and adolescents, together with 25 European research laboratories. **ITTC** launched in 2003, long before the Paediatric Cancer ERN (ERN PaedCan). ITTC is a non-profit organisation established under French Law. The goal is to accelerate the introduction of new, effective, and safe therapies for the treatment of children and adolescents with cancer. The ITTC offers a wide range of collaborations with Industry, across the whole lifecycle of product development, from early portfolio evaluation to advice on generating phase 1 data, through to support with paediatric trial design and finally implementation. In this way, ITTC increases the likelihood of the most effective therapies entering development, optimising the chances of these medicines eventually becoming available to patients.

European Collaboration for Epilepsy Trials (ECET)

This case study concerns a relatively new collaboration across Europe, to improve clinical trials in epilepsies, with strong ERN engagement and leadership

ECET was launched in 2021 by the regional Executive Committee of the International League Against Epilepsy (ILAE-Europe), and was endorsed by the **ERN EpiCARE**, the European Consortium for Epilepsy Trials. The goal is to provide advice and expertise to optimise the design and implementation of clinical trials in epilepsies across Europe, for both adults and children. Despite the approval of numerous antiseizure medications, many individuals with epilepsy syndromes continue to experience seizures, suffer from comorbidities, or experience adverse events. Well-designed trials are essential to provide the necessary

evidence for rational treatment choices in rare epilepsies, but historically, antiseizure treatment trials have been poorly designed. There remains a critical need for well-powered and representative clinical trials to develop novel treatments that can enhance quality of life, reduce seizure burden, minimize adverse effects, lower healthcare costs, reduce the risk of sudden unexpected death, and ultimately, modify the natural evolution of the underlying aetiologies.

ECET is a collaborative group of European investigators with shared interests and a good track record in designing and performing epilepsy trials. These experts have links to over 80 centres across 35 European countries. The priorities include innovative trial design and outcome measures; genetics and targeted therapies; epileptogenesis and disease modification; epilepsy surgery outcomes and follow- up; and more.

ECET offers a range of expert services to both academia and Industry, including the following:

- Leading and supporting natural history studies
- Promoting precision medicine
- Advice on clinical drug development
- Advice on trial design
- Selection of trial sites in Europe
- Centralised/standardised adjudication processes to reduce variability in multicentre trials
- Organising educational activities to enhance the skills of researchers and healthcare professionals.

The ECET is still in its early days, but structures are being develop to contract with pharma companies and CROs. Importantly, the ECET is now an established legal entity.

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ACCELERATE

Another long-established case study from the paediatric cancer community, which centres on multistakeholder meetings

The ACCELERATE Consortium was initiated in 2012, in the paediatric cancer field. The goal is to accelerate the process of developing and evaluating innovative therapies for children and young people with cancer. Pharma companies participate in the activities, which are essentially multistakeholder fora in which the group analyses the state quo of research and development and identifies activities necessary to drive forwards the pace of progress. Industry representatives are part of the Steering Committee, as equal partners, and Industry is part of projects designed to push the field forward (which include education and working groups on clinical research topics, but not specific trials).

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