**Supplement to “Lochmüller et al; Position statement….”**

**SMA Europe Scientific Congress: Workshop/podium discussion on data sharing**   
**Friday 26 January 2018**

Chair: Hanns Lochmuller (Newcastle)

Discussants: Wildon Farwell (Biogen), David Evans (Roche), Francesco Muntoni (London), Nathalie Goemans (Leuwen), Richard Finkel (US), Petra Wilson (Brussels), plus discussants from patient organisations: Marie-Christine Ouillade (France), Vitaliy Matyushenko (Ukraine), Inge Schwersenz (Gemany), Mencia de Lemus (Spain)

Note taking: Jo Bullivant (Newcastle University)

Objectives of the session:

1. Understand which datasets are available in SMA clinical research, and which organizations hold them (beyond scientific publication).
2. What would be desirable for sharing (e.g. data from SMA registries, biobanks, biomarkers, natural history studies, clinical trials)
3. Discuss the opportunities and barriers for sharing such data in relation to stakeholder requirements, practices and views; provide best-practice examples or pitfalls
4. Identify actionable steps for the organisations involved for future research

**Hanns Lochmuller** introduced the workshop by giving a brief overview of the context and importance of data sharing, and discussing some common problems, opportunities, and definitions. He also focussed the discussion towards collection and sharing of clinical research data.

The panellists introduced themselves and each spent 3 minutes sharing their perspective on and experience of data sharing with the group. These introductions are summarised below:

**Francesco Muntoni**Francesco is a paediatric neurologist who works in London and has worked closely with his paediatric neurology colleagues and networks in the UK to develop data sharing projects for both DMD (North Star, which is probably the more advanced one) and SMA (SMA REACH). The latter collects data on outcome measures in SMA, and and has contributed to the development and validation of the Hammersmith Scale for SMA. They are also collaborating with partners to collect outcome data on patients treated with nusinersen. He feels it is highly desirable to work towards an agreed shared minimum dataset for SMA, and that there should not be obstacles to prevent this. He emphasised the importance of using shared definitions and data dictionaries, and stated that ISMAC (International SMA Consortium) would be happy to contribute by sharing their minimum dataset.

**Vitaliy Matyushenko**Vitaliy is the Curator of the Ukrainian SMA Patient Registry. They collect the minimum core dataset of TREAT-NMD which includes natural history data and data from patients on nusinersen. They expect their registry to be used to help with clinical trials.

**Marie-Christine Ouillade**Marie-Christine is the President of SMA Europe and also a member of TREAT-NMD. She highlighted the importance of data sharing as a means of saving a lot of time and money when conducting research. On behalf of SMA Europe she highlighted the possibility of using shared natural history and placebo group data in order to avoid the need for placebo groups in future clinical trials. Many people have already been in a placebo group in different trials, and if we collect and share this data we have a very large existing placebo group for comparison purposes in future trials.

**Mencia de Lemus**Mencia is the Vice-President of SMA Europe and Head of the Spanish SMA Foundation (FundAME) who created the patient-reported Spanish SMA Patient Registry, and started the national consortium for natural history. They are now working on combining the data from these projects and adding new items on Quality of Life (QoL) and other Patient Reported Outcome Measures (PROM). It is in the interests of the patients to make this type of combined data collection systematic and acceptable to authorities. In addition, she is working to incorporate the patient perspective into the datasets for natural history studies. They have identified that there are some data items which might not previously have been looked at by clinicians but which are important to patients and have an impact on their lives. They are also working towards fostering international collaboration.

**Inge Schwersenz**   
Inge is a patient representative on the DGM (Deutsche Gesellschaft für Muskelkranke - the German Society for Muscular Dystrophy) and is also part of SMA Europe and the registry working group. She is also on the oversight committee of the patient-reported German SMA registry which was established when TREAT-NMD started. They have started working with the mainly clinician-reported SMArtcare outcome study, led by the university hospital in Freiburg and including many specialist centres across Germany, to collect data from both treated and untreated patients.

**David Evans**  
David manages the Real World Data team at Roche, who have 2 SMA products in late phase development (olesoxime and RG7916) as well as one in Duchenne. He recognises the importance of clinical trial data, but looks forward as a company to the increasing importance of observational real-world data, and how the two types of data can become complementary over time. As treatments become available in SMA real world data becomes even more relevant, as treatment of the disease actually happens. The SMA community is in a strong position because they have some of the success factors in place: engaged and committed patient groups, very specialised clinical care teams who are experienced in data generation, and lessons learnt from other diseases such as MS. The community should not just rest on existing data efforts such as trials and registries; but to look at what else could be utilised in the data ecosystems (electronic medical records, omics data, imaging data, health economics data, and patient-reported data). Data sharing in a collaborative way should be ambitious as a group effort to bring all these data areas together.

**Wildon Farwell**Wildon leads the clinical development programme at Biogen for nusinersen/Spinraza. Biogen partnered with Ionis and the have the clinical trial data from the nusinersen programme that is still continuing (approximately 250 patients). The trial was initiated in pre-symptomatic infants (NURTURE) and then in symptomatic infants and children (SHINE). They have also partnered with a number of disease registries which they are very committed to. They spoke with regulators from the very beginning and said they didn’t want to create their own industry-owned product-specific registry, they wanted instead to partner with the community make sure that data is available and useful, particularly in rare diseases. So they have been working with different registries to think through what should be the common data elements, what data elements would be of particular interest to different groups. They developed relationships with different members of TREAT-NMD and ISMAC, looking at how that data can be collected and used. They also do post-marketing surveillance where clinicians provide them with safety data which is reported to regulatory agencies and then becomes publicly available.

**Nathalie Goemans**Nathalie is head of Neuromuscular Reference Centre in Leuven and is happy to share her perspective on data sharing at 2 different levels; firstly as a clinical researcher providing data for a natural history study, and secondly as a member of the scientific board for the Belgian neuromuscular disease registry which is affiliated with TREAT-NMD. She serves as Chair of TGDOC (TREAT-NMD Global Database Oversight Committee) which is the network of TREAT-NMD registries which saw many SMA-related activities over the last year. The first purpose of the TRAT-NMD network of registries was to help with assessing trial feasibility and to identify patients who were eligible for clinical trials. However, most of the existing registries are not in a position to provide the collection and timely processing of high-quality, standardized, real world data which is required by regulators for post-marketing safety and efficacy assessment. Biogen supports the development of a new SMA registry platform with partner organizations, including members of the TREAT-NMD Alliance. There need to be strict principles around data ownership and use. This development may also help different SMA registries to harmonise data collection and sharing from an IT perspective. An experienced IT vendor has been selected that also provides the IT platform for the European Reference Networks (ERNs) including EURO-NMD for rare neuromuscular disorders.

**Richard Finkel**Richard is a child neurologist in Orlando, Florida. He participated in a 5-site (Boston, New York, Philadelphia, Orlando and Stanford) network called Pediatric Neuromuscular Clinical Research Network for Spinal Muscular Atrophy (PNCR) which was started 13 years ago and financially supported by the SMA Foundation. Their aim was to develop a clinical trial readiness network in the US. They collected registry and natural history data as if they were running a clinical trial, so in a very systematic way using case report forms. Clinical evaluators were trained and retrained each year, and a central data repository was located at the University of Rochester, where data was collected, carefully assessed, and open for queries. A data sharing relationship was fundamental including the pharmaceutical industry. This was under the assumption that the data would be useful for the drug development and clinical trials, and the data sharing relationship with commercial partners would facilitate clinical trial design. They have also accomplished multiple longitudinal studies, developed new outcome measures such as CHOP INTEND, and explored different imaging, electrophysiological and biochemical biomarkers. They also set up a bio-repository to collect samples of blood, urine, spinal fluid and muscle tissue, and made this available to researchers and pharma. Going forward, it has also been useful to identify patients for clinical trials and for treatment options.

**Petra Wilson**Petra is a lawyer with experience of working with ERNs in rare diseases, where she developed a unified consent system. She stressed the importance of the European GDPR (General Data Protection Regulation) coming into force in May 2018 which is debated mainly for two reasons; either people think it’s going to ruin their work and they will have to change the way they do everything, or they are concerned about something called ‘the right to be forgotten’, which is most famously talked about in the context of social media like Facebook. She wanted to try and allay some fears about the GDPR, because it isn’t going to stop registries, it isn’t going to prevent the collection of natural history data, and it isn’t going to stop people working together. She thinks in fact it will make these research efforts easier because at least at a European level the same rules are applied across all EU member states. There are 2 points where countries may diverge despite the GDPR; (1) Some countries will define the data of a deceased patient as still protected by data protection, and some won’t. (2) The law says that anyone over the age of 13 may give consent, but some countries have made that age limit higher, so it could be anywhere from 13-16. This is important for sharing data across European borders. The concept of FAIR data is very useful as it gets you along the way of collecting data legally. The final point is that informed consent to collecting and using patient data is ethically excellent and desirable, but it’s not the only route legally.

Hanns thanked everyone for their contribution and opened the floor up for question or discussions:

* A workshop attendee asked about the lack of guidance in the GDPR around anonymisation of genetic data.   
  Petra Wilson suggested that in rare diseases (and in medical data generally) there is no point talking about anonymisation. Taking off identifiers like names, dates of birth, NHS numbers and so on, is not sufficient to anonymise. What you can do is pseudonymise, which brings you into a lower threshold of security levels and would be a very good counter-balance for not having patient consent. Anonymisation is not a legally viable option in your field.
* Hanns Lochmuller asked about the idea of sharing placebo data from clinical trials as it seems to be a clear and understandable request from patient organisations. Are there opportunities to do this? Has it been successfully done in the past?
  + Francesco Muntoni answered that the EMA encouraged companies to do this at a workshop 1 year ago. Also, as there are not many clinical trials at moment with placebo arms – is it avoidable going forward? In DMD, regulators have approved drugs in some cases based on historical controls, but it is not clear how well this data matches with true placebo data. Standardisation and quality control of data captured in natural history studies could help towards the goal of reducing as much as possible the need of large placebo arms in studies.
  + David Evans agreed that we all share the goal of not needing placebo arms. From a Roche perspective they do have a clear policy on patient data sharing for legitimate research purposes. He also mentioned experience in other areas, for example TransCelerate, where there are efforts to pool placebo or standards of care data and make that accessible to participants. This requires a lot of investment effort going into data curating, interoperability, and re-coding so that the data is easy for researchers to use, and there are not ad-hoc decisions being made after the data gets out there.
  + Wildon Farwell said that Biogen has placebo/sham data in SMA, and they have a policy similar to Roche which makes it possible to share data, upon review of the type of project and how the data sharing will occur. They are operating in very regulated environment. Clinical trials use Informed Consent Forms (ICFs) which include restrictions what we can do with the data, how long we can have it for, and other things that have to be taken into account. Competitive considerations are also relevant for companies in drug development. Biogen want to be good partners and to be part of the conversation and solution but must keep all factors in mind. It is also important to say that regulators have sham controlled data from trials, safety reporting etc. so there is also an opportunity for regulators/payers to share data under appropriate guidelines.
  + Petra Wilson said that in relation to using data in a way that wasn’t the primary intent when the data was collected (e.g. it was collected in the placebo arm of a clinical trial and now you want to use it differently), this is where you come into issues with the law about specific consent. There is a slow but growing movement to adopt a model called dynamic consent – where you inform patients about studies coming up, or potential other uses of their data, and give them the option to opt in. This concept is relatively new and is not strictly speaking provided for in the legislation, but most regulators are beginning to think it is the way forward.
* A workshop attendee asked for clarification on ownership of data when it is being shared in a much wider way than before – where if you have additional funding coming in you might have ownership of the database versus ownership of the data originally provided.
  + Petra Wilson highlighted the distinction between the source of data (patient) and what happens to data afterwards. Regarding ownership of data, it’s important to realise that raw data (e.g. tissue sample, data taken directly from the patient) is simply that - just data. It is the later work of others that turns that data into information and knowledge. In law, there is no ownership at data subject level, so the patient has legally no ownership over the data (this doesn’t mean they don’t have interest, or rights to access, right to correction, right to portability). Ownership accrues from the work; i.e. as you add value to data by doing something to it. So whilst there is a notion of moral ownership for the data subjects, this is not a legal concept. Nevertheless, they have important rights that need to be respected. How structured relationships of ownership when many people have added value to data is protected under intellectual property law (e.g. concept of foreground and background intellectual property).
* Hanns Lochmuller highlight good examples of where data sharing has occurred and facilitated progress and better outcomes for patients, e.g. the initiatives explained by Richard and Francesco. He stated that for certain types of research, there is a need to pre-specify very clearly what the format and standard of the data is required, eg on Case Report Forms (CRFs) etc. What is coming next in terms of outcome data for treated patients?
  + Richard Finkel answered that the concept in the PNCR group was to identify the data that would be necessary if the patient was actually in a clinical trial. That meant understanding 3 basic areas; the first was the genotype and related biomarkers, the second was careful characterisation of phenotype and how to measure changes over time (longitudinal study). For the third they tried to be forward-thinking and asked “if this was a clinical trial, how would we capture that data?”. So they carefully scripted and defined their case report forms in the database meaning that there was no room for opinion or words. Everything was defined as Yes/No, or 1/2, so that every site was collecting data in the same way and it could be aggregated and interpreted to mean something fairly uniform. That wasn’t always the case but that was the goal. Over time they started working collaboratively with Francesco’s group in the UK and Eugenio (Mercuri’s) group in Italy. They found that they had the same ideas, and they meant more or less the same thing, but it did a lot of work to align things. Going forward they are formulating the ISMAC group, to find out if they can make this work at an international level and merge different datasets. Ideally this would then be opened up more globally and not be kept as a closed group.
* A workshop attendee asked what the next steps should be to allow better data sharing. What should we go out and do next?
  + Richard Finkel suggested that it’s about collecting different types of data at different levels. We’ve heard about the ISMAC work which is highly curated, high level data. But it’s also about collecting real world data from a variety of sources. They are trying to align as closely as possible with TREAT-NMD and others globally so that data from different sources can be merged together. Hopefully this will involve us all meaning the same thing, using the same common data elements, the same data dictionaries and so on.
  + Nathalie Goemans agreed that harmonisation of the data collection is key but also drew attention to the practical considerations such as validation of measures and methods.
  + Wildon Farwell added that from the clinical trial perspective the real challenge is technology and trying to get ahead of it. Data collection technology is moving so fast that it is hard to keep up with that and incorporate it into conversations with regulators and payers.
  + David Evans agreed and proposed a bottom up approach to get the core data set for outcome research and postmarketing right. He suggested that the data needs to be curated and reliable. The value of that data needs to be demonstrated – this is where patient groups and the research community come in to show the impact of the data. Optimistically, this would ultimately feed into policy and legal frameworks.
  + Petra Wilson added that every organisation involved with data collection can help drive the data sharing agenda by making interoperability part of the procurement process when software or technology for data collection is purchased, and building the standards in from the outset.
* A workshop attendee asked for further clarification, because you might have a high quality dataset and lots of data, but on the other hand you can’t anonymise it and therefore can’t share it – what are the steps? And what does the patient get back out of this?
  + Petra Wilson responded that you don’t need to anonymise data. If you do anonymise it, the law doesn’t apply and therefore you can do what you like with it. It is almost impossible to anonymise data about disease like SMA, but what you can do is have good security in place and a good reason for sharing it, e.g. for treating patient or doing research.
* Hanns Lochmuller asked Marie-Christine Ouillade to make a statement about what patients and patient organisations want. Marie-Christine summarised that patients need access to their own data and now it is their legal right. An additional opportunity for data sharing, that does not require anonymization of individual level data, is sharing and comparing aggregated data. A possible way forward is for the database with individual level data to remain confined to local hospital or national level, but to share aggregated data at any level and more widely where it is helpful for research, standards of care and many other purposes. The patient community considers data sharing an important and urgent priority.

Hanns Lochmuller thanked everyone for a lively discussion, acknowledging that probably not everybody agrees with everything that has been said but that it is important to understand the viewpoints and objectives of different stakeholders. It is clear as an outcome that there is a huge willingness from all stakeholders to make this work for SMA and share data for the benefit of patients.