TREAT-NMD SMA Registries Dataset Pilot Workshop 2 Report

11-12 June 2018

Newcastle, UK

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1. DISCLOSURE AND CONFLICT OF INTEREST

This workshop was part of the TREAT-NMD SMA Dataset Pilot Study supported by Biogen; a pharmaceutical company with an approved therapy (Spinraza) for spinal muscular atrophy (SMA).

This report was prepared by the Pilot Study Project Manager and Newcastle University employee; Jo Bullivant, with review and input from the TGDOC Chairs (TREAT-NMD Global Database Oversight Committee), the TREAT-NMD Secretariat, and the TGDOC SMA Sub-Group leads.

TGDOC Chairs:

- Nathalie Goemans (Chair)
- Craig Campbell (incoming Chair)
- Hugh Dawkins (outgoing Chair)

TREAT-NMD Secretariat:

- Jo Bullivant (SMA Dataset Pilot Project Manager)
- Joanne Lee (Postmarketing Surveillance Project Assistant)
- Julia Stickland (TREAT-NMD Coordinator)
- Rebecca Leary (EURO-NMD Project Manager)

TGDOC SMA Sub-Group Leads:

- Miriam Rodrigues (New Zealand Neuromuscular Disease Registry Curator)
- Victoria Hodgkinson (Canadian Neuromuscular Disease Registry Curator)

This report provides an overview of the discussions and resulting recommendations made during Workshop 2. It does not necessarily represent the full perspectives of any individual attendees, Biogen, or TREAT-NMD.

2. EXECUTIVE SUMMARY

In 2017, TREAT-NMD identified a need to review and alter the data items collected within the core dataset of the TREAT-NMD global SMA registry. This was with the aim of better informing the understanding of the natural history of SMA, providing context to understand the safety and effectiveness of new treatments, and supporting post marketing surveillance (PMS) for emerging new treatments through a disease-specific rather than drug-specific approach.

A proposed expanded dataset was developed during Workshop 1 in May 2017. Following the recommendations from this workshop a sub-group of 12 TREAT-NMD SMA Registries (Pilot Sites) commenced a trial implementation (Pilot Study) of the proposed expanded dataset, and provided ongoing feedback on its feasibility.

The objective of Workshop 2 was to bring together the 12 Pilot Site Curators and review all feedback collected throughout the Pilot Study to date; from both the Pilot Group and other relevant initiatives. The intended workshop outputs were:

- Final recommendations from the Pilot Sites on the content and structure of the expanded TREAT-NMD SMA dataset, for consideration and final approval by the TGDOC Chairs.
- Perspectives and input to inform the full-scale implementation plan, which is the proposed next phase of this work.

2a. Key findings:

- The expanded TREAT-NMD SMA Dataset must be:
    a. Appropriate for all sizes and types of registries in the network, including patient-reported.
    b. Accessible and not off-putting for new registries interested in joining the network.
    c. Aspirational for those with capacity or expansion plans.
    d. Comparable with other data collection initiatives

- The Pilot Group recommend:
    a. A single dataset for all types of registry, split into mandatory and highly encouraged items.
    b. That TREAT-NMD SMA Registries should be required to include the mandatory items in their case report forms, and make every effort to collect them (or agree actions to work towards their collection).
    c. That the minimum data needed for an individual record to be accepted as valid for any global registry enquiry should be defined on a case-by-case basis.
    d. That some mandatory items apply only to clinician-reported registries, some only to patient-reported registries, but the majority apply to both. The above-mentioned exceptions will be clearly marked in the dataset.

- The following additional data items were considered and recommended for inclusion. These items were not originally included in the proposed expanded dataset, and therefore have not been piloted for feasibility during the Pilot Study:
    a. Method of genetic testing and screening programme details.
    b. Head and chest circumference, height and weight.
    c. Treatment dosing schedule adherence.
    d. Reported serious adverse events (SAEs)

- Following Workshop 2, the discussions and recommendations were developed into dataset documents and circulated to participants for review. Once the feedback has been consolidated, the dataset will be submitted to the TGDOC Chairs for review and final sign-off, and confirmed in the Final Pilot Study Report at the end of August.

- The second output from Workshop 2 was a set of recommendations on the following aspects of the implementation plan to roll out the expanded dataset to the full network of TREAT-NMD SMA Registries:
    a. Scoping – what do we need to find out about the other registries?
    b. Training and support requirements for registries – how can we identify and meet them?
    c. Data quality - how to ensure it and demonstrate it?

  The implementation plan will also be confirmed in the Final Pilot Study Report at the end of August.

- In acknowledgement of the rapid developments in the current SMA landscape a formalised 'dataset amendment plan' is recommended, to support continued engagement and harmonisation of the TREAT-NMD work with other SMA data collection initiatives and the wider SMA community.

3. ABOUT THE WORKSHOP

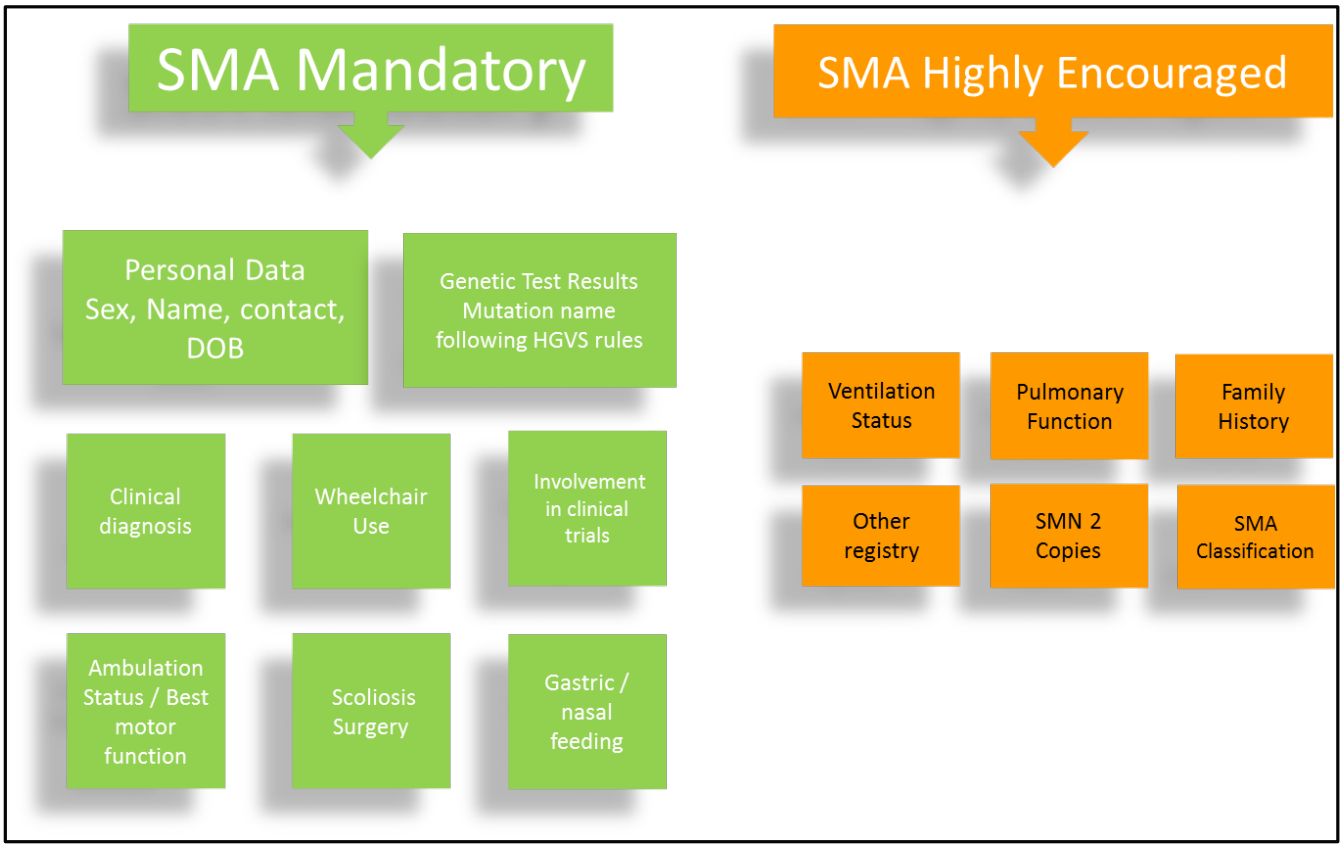
3a. Context and background

Spinal Muscular Atrophy (SMA) is a rare, genetically inherited neuromuscular condition which causes progressive muscle weakness and loss of movement due to muscle atrophy. There are different types of SMA, and a wide spectrum of how severely patients are affected.

Biogen is a pharmaceutical company with a treatment for SMA, SPINRAZA® (nusinersen), which has been approved by the Food and Drug Administration (FDA) for use in the US and by the European Medicines Agency (EMA) for use in Europe.

The TREAT-NMD Global Network of SMA Registries collect a common core dataset, made up of mandatory and highly encouraged data items.

Figure 1: Current set of mandatory and highly encouraged data items



In 2017, TREAT-NMD identified a need to review and alter the data items collected within the core dataset of the TREAT-NMD global SMA registries in order to:

- Improve the quality and quantity of natural history / longitudinal SMA data.
- Provide context for understanding safety and effectiveness of Spinraza and other emerging treatments
- Provide data to support the post-marketing surveillance (PMS) of Spinraza and other future therapies through a disease-specific rather than drug-specific approach.

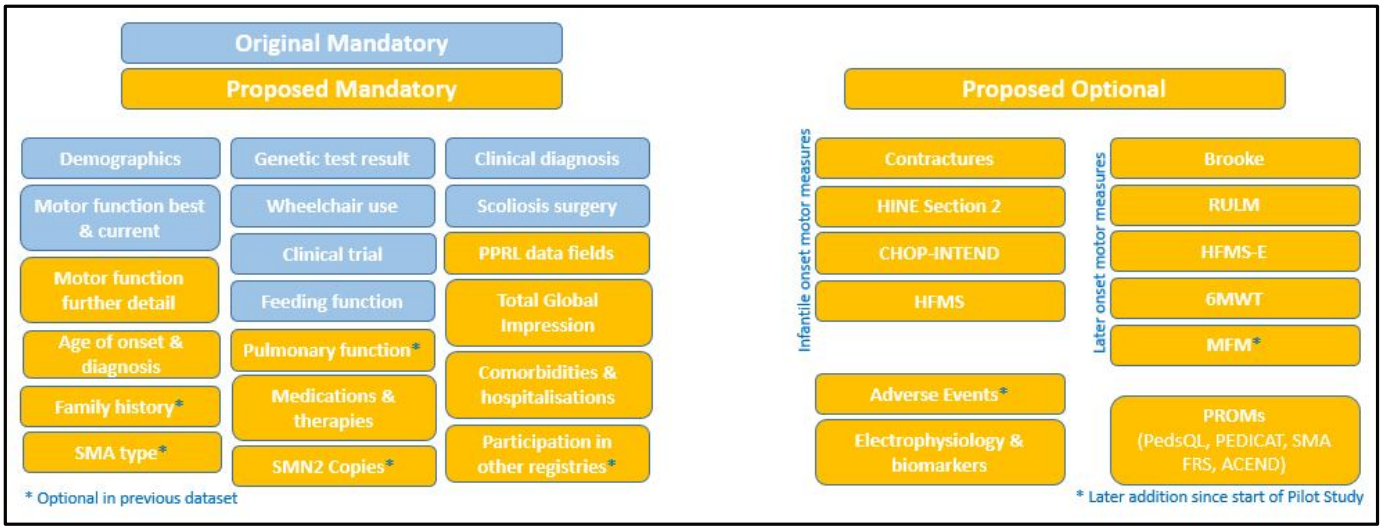
In May 2017, Workshop 1 was held in Amsterdam, Netherlands. The intention of this workshop was to:

- Gather input from key stakeholders in the SMA community

- Build consensus around which data items are appropriate to be added
- Highlight practical factors to be taken into consideration.

The intention was not to make any final decisions; rather to produce a collective set of well-thought-out suggestions for consideration by the TGDOC Chairs. The output was overall consensus on a categorised list of 38 items for consideration for inclusion into the Global SMA Registry core dataset; prioritised and assessed against a feasibility matrix.

Figure 2: Proposed expanded SMA dataset for consideration



Based on the recommendations from Workshop 1, a sub-group of 12 TREAT-NMD SMA Registries (Pilot Sites) volunteered and were judged appropriate to pilot the proposed expanded dataset, and agreed to provide ongoing feedback on its feasibility during the Pilot Study. A bursary of up to €8,000 per Registry was made available to Pilot Sites in acknowledgement of the additional time, resource and sometimes software development implications.

Feedback was collected from the Pilot Sites on an ongoing basis, as described in the "TREAT-NMD SMA Registries Dataset Pilot Study: Progress Report 2" which was submitted to Biogen on 1 June 2018.

In order to generate the final recommendations from the Pilot Group on the expanded SMA dataset, Workshop 2 reviewed a culmination of feedback received throughout the Pilot Study to date, from:

- Pilot Site Curators (Pilot Group)
- TREAT-NMD SMA Universal Platform Working Group
- International SMA Consortium (iSMAC)
- SMArtCARE

The membership of the groups above is summarised in Appendix A. Feedback from other interested parties such as non-pilot TREAT-NMD SMA Registries and patient organisations was also gathered and reviewed.

3b. Methodology and pre-work

As described in Progress Report 2, a schedule of formal and informal feedback collection laid the groundwork for Workshop 2, as described below:

December 2017: A survey asked Pilot Site Curators about the implementation status of the expanded dataset and their concerns.

March 2018: Pilot Site Curators were contacted individually to provide the following information:

- Any further progress made since the previous feedback was provided
- A specific update on any concerns they had previously reported
- Whether they were experiencing any problems with implementing the dataset before the end of the pilot, and if so, whether we could do anything to help overcome them

As part of the Pilot Site Bursary claim approval process, Curators were also required to submit additional feedback; details of which are available in Progress Report 2.

May 2018: Individual telephone interviews were conducted by the Pilot Study Project Manager with each Registry Curator, to gather detailed feedback on each data item.

4 June 2018: A webinar was held to present and summarise feedback collected during the pilot study to date, to all Workshop 2 invitees. The purpose of the webinar was to:

- Provide the extensive feedback information in advance of Workshop 2; thereby allowing participants time to reflect and consider their opinions.
- Set the scene for Workshop 2 and the decisions that would need to be made.
- Allow Workshop 2 to focus on discussion and decision-making rather than information-giving.
- Allow those who were unable to attend Workshop 2 the opportunity to take part and provide any input ahead of the workshop.

The webinar was recorded and made immediately available (along with the slides and all associated documents) for anyone who was not able to join live. The slides are provided in Section 5 (Presentations).

Following the webinar, participants were asked to reflect on all of the feedback presented, and to consider their approach to the decisions that would need to be made at Workshop 2.

11-12 June 2018: Workshop 2 was delivered by the Pilot Study Project Manager with the support of the same external, impartial, freelance facilitator who supported Workshop 1.

3c. Workshop agenda and structure

Workshop 2 was structured with the intention of ensuring that:

- Every participant had opportunity to provide their opinion where they wished; including those who were not able to be physically present.
- Participants had the opportunity to challenge anything they were unsure of, and change their preferences or opinions after listening to input from other participants.
- A clear decision was reached (or further actions agreed) for each element of each individual proposed data item.

The facilitator outlined clear 'ground rules' at the start of the workshop, which set the scene for open, collaborative and inclusive discussions.

The agenda was intended to be flexible to respond to the course and pace of decision-making.

Figure 3: Workshop 2 Agenda

Monday 11th June 2018		
09:00	Welcome, introductions, setting the scene	Jo Bullivant & Nathalie Goemans
09:20	The Biogen perspective	Sue Hall
09:30	Workshop scope and purpose Recap from Webinar	Facilitator Jo Bullivant
10:15	Decision-making	Jo Bullivant & Facilitator
16:00	Sense-check: overall feasibility of complete dataset	Jo Bullivant
17:00	Round-up of Day 1	Facilitator
Tuesday 12th June 2018		
09:00	Review of Day 1 progress and agreed actions	Facilitator
09:30	Group work: Implementation planning	Facilitator
12:30	Conclusions, next steps, final remarks	Nathalie Goemans

Participants were reminded of the scope of the workshop:

- Decision-making based on information available
- Action-planning in case of any information not yet available
- Further feedback still possible (final report 30th August)
- Collaborative & open: for the benefit of the SMA community
- In case of no consensus; TGDOC Chairs' final decision

Not in scope, although related to discussions, was the Universal Platform project.

3d. Workshop 2 decisions

During the decision-making segment of the agenda, the participants worked in one large group. The facilitator asked for their opinion (and guided them to a consensus if necessary), on the following decisions:

- Is a tiered structure appropriate for the new expanded dataset, to reflect the diversity in capacity and resource of the TREAT-NMD SMA registries?
    - If so, what should it look like?

- For each individual data item in the proposed expanded dataset:
    - Should it be included at all?
        - If not, why not?
    - If so:
        - Mandatory or optional?
        - Which tier (if a tiered structure is agreed?)
        - When should it be collected; baseline only or follow up?
        - If follow-up; frequency of data collection?
        - Wording and definitions, including coding of responses

Before each decision was recorded, individual participants indicated their level of approval by holding up one of three coloured cards; a green card signified approval, yellow signified general agreement but with some reservations, and red indicated disagreement. This allowed the discussions to focus on areas lacking consensus, whilst progressing as quickly as possible and not overlooking or disregarding any individual concerns.

At the end of these discussions, the resulting dataset was examined as a whole to ensure that it was deemed realistic and feasible. This was based on the acknowledgement that judging each individual item to be feasible does not automatically indicate that the dataset as a whole is feasible.

During the final segment of Workshop 2, participants broke into 3 groups, with each group discussing a different aspect of the full-scale implementation plan (see figure 4 below). Following the discussions, each group fed back to the other workshop participants.

Figure 4: Implementation planning groups

Group 1:	Scoping – what do we need to find out about the other registries? (E.g. key factors/barriers, timeline, cost, critical path analysis)
Group 2:	Training/support requirements: (Bespoke training courses? Masterclasses? Toolkits? Licenses? Collaboration with other groups? Online?)
Group 3:	Data quality: how to ensure it and demonstrate it? Stakeholder mapping & communications planning

3e. Workshop participants

Chairs / Organisers:

1. Nathalie Goemans, TGDOC Chair
2. Craig Campbell, TGDOC Chair Elect
3. Jo Bullivant, Pilot Project Manager
4. Craig Smith of Flint Spark Consulting, Independent Facilitator
5. Joanne Lee, Postmarketing Project Assistant

Pilot Site Registry Curators

Nathalie Goemans (Belgium)

6. Victoria Hodgkinson (Canada)
7. Rasha el Sherif (Egypt)
8. Aurélie Chabanon (France)
9. Marcel Heidemann (Germany Munich)
10. Venkataraman Vishwanathan (India)
11. Miriam Rodrigues (New Zealand)
12. Damjan Osredkar (Slovenia)
13. Lindsay Murphy (UK/Ireland)
14. Vitaly Matyushenko – joining via GoToMeeting (Ukraine)

TREAT-NMD Secretariat

15. Anne Oyewole, Postmarketing Surveillance Coordinator & SMA Universal Platform Lead
16. Julia Stickland, TREAT-NMD Coordinator
17. Rebecca Leary, EURO-NMD Project Manager
18. Nicole O'Connor, TREAT-NMD SMA Education Coordinator

Biogen

19. Sue Hall
20. Aisha Rashid

Apologies from:

- Melanie Barth (Biogen)
- Robert Bezar (Biogen)
- Adrien Bretagne (Biogen)
- Hugh Dawkins (Outgoing TGDOC Chair)
- Michelle Farrar (Australia)
- Rob Hyde (Biogen)
- Jan Kirschner/Kirsten König (Freiburg, Germany)
- Jenifer Loscher (Biogen)

4. WORKSHOP DISCUSSIONS

The workshop discussions were designed to highlight areas of consensus, resolve areas of disagreement, and take into account wider feedback in order to reach a decision on each item.

4a. Tiered structure

It was proposed to the group (and agreed) that the expanded TREAT-NMD SMA Dataset must be:

- Appropriate for all sizes and types of registries in the network, including patient-reported.
- Accessible and not off-putting for new registries interested in joining the network.
- Aspirational for those with capacity or expansion plans.
- Comparable with other data collection initiatives.

After discussion and consideration of different options proposed, the group recommended a single dataset for all types of registry, but split into mandatory and highly encouraged items. After further clarification, it was also recommended that:

- TREAT-NMD SMA Registries are required to include the mandatory items in their case report forms, and make every effort to collect them (or agree actions to work towards their collection).
- The minimum data needed for an individual record to be accepted as valid for a global registry enquiry will be defined on a case-by-case basis.
- Some mandatory items will apply only to clinician-reported registries, some will apply only to patient-reported registries, but the majority will apply to both. The above mentioned exceptions will be marked in the dataset.

4b. Data item recommendations

During the pre-workshop webinar, the Pilot Study Project Manager presented a table of the data items which included consolidated feedback on each one. This table was used as an open working document during Workshop B, as a means of recording the decisions made against the questions defined in Section 3d of this report (Workshop 2 decisions).

During the Pilot Study, certain additional data items had been suggested for inclusion which were not originally part of the proposed expanded dataset, and were therefore not being piloted. Any suggestions received were considered and discussed by Workshop 2 participants, and the following additional items were recommended for inclusion:

- Method of genetic testing and screening programme details.
- Head and chest circumference, height and weight.
- Treatment dosing schedule adherence.
- Reported SAEs

A sample of the working document is shown in figure 5 below, and a full copy as it looked at the end of the workshop is available in appendix B.

Following the workshop, the Pilot Study Project Manager used the working document and the workshop notes taken by the Postmarketing Project Assistant to generate the following dataset documents:

- A high-level overview of the recommended dataset (appendix C)
- The full recommended expanded dataset from the Pilot Group (sample shown in figure 6 below, full document available in appendix D)

Review of these documents will therefore illustrate the decisions and recommendations that the group agreed during the workshop, and the Pilot Study Project Manager's interpretation of these into the 'clean' dataset documents in appendices C and D.

The dataset documents were sent to the workshop participants for review and comment, for which the deadline was Friday 20 July 2018. After incorporating any comments or corrections received, the documents will be submitted to the TGDOC Chairs for final approval and sign-off, and the new expanded dataset will be confirmed as part of the Full Pilot Study Report and Implementation Plan on 30 August 2018.

Figure 5: Sample section of the Workshop 2 working document:

Data item	Data item description	Coding	Baseline	Follow-up	Tier	Comments
4. Clinical Examination						
4.1	Age of symptom onset *-need definition (at what age was it suspected something might be different? Prenatal; at birth; or age MM/YYYY (SMArtCARE)	Months from 0.5 Years and months (can be approx.)	X		M	iSMAC (Date)
4.2	SMA type ⌂ *	0; 1; 2; 3; 4; ~~Other (please specify)~~	X		M	Platform iSMAC (Don't record 'Other') Should we use the same definitions as iSMAC (data dictionary p10)? YES
4.3	Height/length in cm *Add method of height measurement	Numerical value	X	X		Platform iSMAC (metres)
4.4	Weight in kg	Numerical value	X	X		Platform iSMAC
4.5	Head circumference in cm Infants only (<24 months)	Numerical value	X	X		Platform iSMAC
4.6	Chest circumference in cm at full expiration Infants only (<24 months)	Numerical value	X	X		Platform iSMAC (Just 'Chest circumference in infants')
4.7	Chest circumference in cm at full inspiration Infants only (<24 months)	Numerical value	X	X		Platform As above
	CONTRACTURES X		X	X		
4.8.0	Shoulder contractures	~~Right; left~~ X				
4.8.1	Elbow contractures	~~Minimal; Moderate; Severe~~				Platform
4.8.2	Wrist contractures	~~*Define?~~				
4.8.3	Finger contractures					
4.8.4	Hip contractures	Yes; No				
4.8.5	Knee contractures					
4.8.6	Ankle contractures					Platform

Figure 6: Sample section of the recommended expanded dataset now under review:

Black = mandatory
Blue = highly encouraged
CR = mandatory only for clinician-reported registries
PR = mandatory only for patient-reported registries

Section 10: PULMONARY FUNCTION

Item no.	Data item description	Coding	Baseline	Follow-up
10.00	Has the patient ever used invasive ventilation?	Never; Previously (start and end date MM-YYYY); Currently (start date MM-YYYY); Unknown	X	X
10.01	If 'Yes' to 10.00: Frequency of invasive ventilation	Full-time; part-time; unknown	X	X
10.02	If 'Yes' to 10.00: Invasive ventilation start date (month and year)	MM-YYYY	X	X
10.03	Has the patient ever used non-invasive ventilation?	Never; Previously (start and end date MM-YYYY); Currently (start date MM-YYYY); Unknown	X	X
10.04	If 'Yes' to 10.03: Frequency of non-invasive ventilation	Full-time; part-time; unknown	X	X
10.05	If 'Yes' to 10.03: Non-invasive ventilation start date (month and year)	MM-YYYY	X	X
10.06	Does the patient need assistance in airway clearance and/or secretion mobilisation?	Yes; No	X	X
	If 'Yes' to 10.06; Type of assistance (select all that apply)			
10.07	Suction	Daily; Weekly; Occasionally	X	X
10.08	Chest percussion	Daily; Weekly; Occasionally	X	X
10.09	Cough Assist device	Daily; Weekly; Occasionally	X	X
10.10	Other (Please Specify)	Daily; Weekly; Occasionally	X	X
10.11	Has the patient had a Forced Vital Capacity (FVC) test?	Yes; No; Unknown	X	X
10.12	If 'Yes' to 10.11: Date of most recent FVC test, if known	DD-MM-YYYY	X	X
10.13	CR If 'Yes' to 10.11: FVC litre	[Numerical value]	X	X
10.14	CR If 'Yes' to 10.11: FVC predicted % as calculated in your local lab	[0-150] %	X	X

4c. Points of interest

In addition to the confirmation of the final recommendations provided in the dataset documents described in section 4b, it is also useful to summarise particular areas of discussion in order to explain the recommendations that were agreed.

i. Registry Enrolment and Demographics

It is assumed that individual registries already record this information as a matter of course, however it was also judged important for individual registries to be able to centrally report enrolment and consent information in a standardised way, to facilitate the monitoring of quality and compliance of the TREAT-NMD SMA Registries.

The majority of the recommended demographic items in the expanded dataset constitute personal data under Data Protection Laws, and therefore would never be requested for central submission. Nevertheless it was judged important to provide registries with guidance on which demographic items should be collected for their own internal use, and in particular with a view to future compatibility with PPRL technology (Privacy Preserving Record Linkage).

ii. Genetic diagnosis

It was proposed by the group that the method of genetic testing (including the method of SMN2 copy number testing) should be collected wherever possible. In addition, the group felt it was relevant to give the option to record whether the genetic diagnosis was made through a screening programme, and if so what type of programme.

iii. Clinical observations

The following new additions were proposed and agreed for inclusion as optional items:

a. Height/length (cm)
b. Method of height measurement
c. Weight
d. Head circumference (for infants <24 months old)
e. Chest circumference at full expiration (for infants <24 months old)
f. Chest circumference at full inspiration (for infants <24 months old)

In the proposed expanded dataset, contractures were reported according to which side (left or right) they affected. It was agreed that this was not relevant information and so they are now simply recorded as present or not. Since Workshop 2 a further suggestion has been received from a member of the iSMAC group, to add a simple 3-item scale against each contracture to report how severely the patient's range of motion is affected. This will be proposed to the TGDOC Chairs in the final dataset.

iv. Motor function

Certain items in this section have been included in order to be able to derive a WHO score in the absence of any other validated motor measure (for example if a small or new registry is working towards the implementation of their first motor outcome measure). However, it is important for the sake of data analysis to acknowledge that the motor functions reported in this section could potentially be anecdotally reported by a patient or caregiver, rather than observed by an appropriately trained healthcare professional. It is therefore recommended that for each function we record whether it was observed or reported (and if reported, by whom).

v. **Therapies and medications**

One notable addition was made to this section, which was to record whether the patient was following the recommended dosing schedule, and if not, the reasons for this.

vi. **Hospitalisations and comorbidities**

There was significant discussion around whether comorbidities should be included as mandatory or highly encouraged. The consensus reached, based on guidance received from the EMA about what will be important for post-marketing surveillance, was to include comorbidities as mandatory.

For the same reason it is also recommended that for each acute hospitalisation or comorbidity reported, the person reporting it is asked to indicate whether it was also reported as a Serious Adverse Event (and if so, in relation to which medication.

vii. **Motor measures**

There is currently a great diversity of opinion across SMA field on the suitability of different motor outcome measures. As a collaborative project, TREAT-NMD must try to remain neutral and inclusive whilst providing impartial guidance where needed. Therefore, if a validated motor measure is already in use by a registry, they should be able to report it to the TREAT-NMD Global Registry. Selection of appropriate motor measures is left to the discretion or preference of clinicians and/or their patients. Where there is no pre-existing preference, the following measures are suggested by TREAT-NMD based on current Standards of Care and prior use in Clinical Trials.

<u>Infantile onset SMA</u>
CHOP-INTEND
HFMS
<u>Later onset SMA</u>
HFMS-E
RULM

The Pilot Group were mindful of the burden of collecting motor outcomes measures, and so it is recommended that registries should be mandated to collect a minimum of 1 validated motor measure.

The dataset manual in development will be harmonised with iSMAC and other data collection initiatives.

It is recommended that the WHO score in this section should only be reported if derived by a healthcare professional by observing the relevant motor functions (whereas the motor functions reported in the Motor Function section could potentially be anecdotally reported by a patient or caregiver).

viii. **Patient-reported outcomes (PRO)**

Of the PROs included in the proposed expanded dataset, only 1 was judged feasible for mandatory inclusion by all Pilot Sites, and this was the Total Global Impression (TGI). This validated scale can easily be embedded within registries and needs no training or licensing.

Collection of any other PRO is recommended to be at the discretion of individual registries, and all of the validated PROs currently used (or suggested) by the Pilot Sites are included as options in the expanded dataset. In addition, Patient Organisations should be consulted on, and involved in, the ongoing work to identify and incorporate appropriate patient-centred outcome measures (PCOM).

4d. Wording and coding

Workshop 2 participants recommended that a patient-friendly version of the dataset wording is produced, for use by patient-reported registries. This should be supported be a patient-facing equivalent of the dataset manual, to support patients and encourage accurate data reporting.

Registries who choose to host on the TREAT-NMD Universal Platform will benefit from the embedded MedDRA code auto-complete look-up function, for hospitalisations and comorbidities. For registries not hosted on the Universal Platform, picklists will be provided.

4e. Implementation planning

Workshop 2 participants split into 3 implementation planning groups as described in figure 4 (section 3c). Images of the flip chart pages produced by each group are provided in Appendix E, and the key themes are summarised below:

Group 1: Scoping
(Victoria Hodgkinson, Marcel Heidemann, Lindsay Murphy, and Nathalie Goemans)

What should we ask the other SMA Registries in order to scope out the full-scale implementation plan?

- Clinician or patient reported
- Comparison/mapping of datasets to identify feasibility/overlap and compatibility of expanded dataset
- Current IT platform usage
- Ethical considerations (amendments, re-consents, timeline, manpower)
- Barriers (money, personnel, dataset feasibility, data entry, translations)
- Patient numbers
- Individual implementation plan
- Geographical representation

Group 2: Training and support
(Sue Hall, Anne Oyewole, Rasha el Sherif, Aurélie Chabanon)

What training or support considerations or provisions should there be?

- Multi-stakeholder
- Bespoke courses / tailored to regional needs
- Registry/dataset masterclass linked to main masterclass
- Tools
- Biogen app / online training
- Accreditation
- Manuals for motor measures, data collection and data entry
- Licenses
- Grant funding (patient organisations, industry)
- Differences in standards of care, particularly between USA and other countries

Group 3: Data quality & stakeholder/communications mapping
(Aisha Rashid, Miriam Rodrigues, Venkataraman Vishwanathan, and Craig Campbell)

What can we consider putting in place to improve/ensure/demonstrate data quality?

- Training (mentoring, data dictionary)
- Internal and external monitoring and audits
- Governance
- Protocols & SOPs
- Motor outcomes metrics agreement
- Checklist
- Toolkits
- EMA Certification
- Use IT platform
- Communications plan and trouble-shooting

What/who should we consider when mapping out the stakeholder communications plan?

- Patients
- Patient advocacy groups and families
- Healthcare professionals (clinicians, physiotherapists, allied health)
- Public health / government
- Health technology assessment (payers)
- Industry
- Regulatory authorities
- Researchers
- Neuromuscular networks
- Formation of a Publications Committee
- Appointment of a Communications Officer

5. PRESENTATIONS

5a. **Webinar slides (4 June 2018)**

5b. **Workshop 2 slides (11-12 June 2018)**

6. CONCLUSIONS AND NEXT STEPS

6a. Conclusions

Workshop 2 achieved all of its stated objectives, and the outcomes were;

- A clear recommendation from the Pilot Group on the contents and structure of the expanded TREAT-NMD SMA dataset.
- Guidance on considerations for the full-scale implementation plan.

Concerns around capacity and resource of the different TREAT-NMD SMA registries were addressed by separating data items into mandatory and highly encouraged categories, and by recommending that registries who cannot straight away implement all the mandatory items should be supported to put in place an action plan to work towards it. It is important to note that the recommendations made in the workshop have not finalised the expanded dataset, and that the final approval and sign-off will be given by the TGDOC Chairs. However, no major revisions are anticipated before approval.

It is also important to acknowledge that although overall consensus was reached on all recommendations, there were some areas of strongly differing opinion within the group and it stands to reason that this will also be the case in a wider audience. In addition to this the SMA landscape is evolving rapidly, and TREAT-NMD wish to remain open to improvements and collaboration or harmonisation with other initiatives. Therefore, a 'dataset amendment plan' is also recommended to provide a formalised and streamlined process through which interested parties can propose amendments to the dataset in the future.

6b. Next steps

It is now proposed that:

- The expanded dataset based on the recommendations from Workshop 2 will be given final approval and sign-off by the TGDOC Chairs. This will lock-down the dataset for any further amendments outside of the dataset amendment plan recommended above. The final dataset will be confirmed in the Final Pilot Study Report on 30 August 2018.

- A scoping exercise is conducted with the TREAT-NMD SMA Registries who were not involved in the Pilot Study, to inform the full-scale implementation plan. This full-scale implementation plan will also be confirmed in the Final Pilot Study Report on 30 August 2018.

- The full-scale implementation should be initiated as soon as is feasible, in order to maintain the momentum of the project.

7. APPENDICES

Appendix A: Membership of Relevant Groups

Pilot group:	Universal Platform (OpenApp) working group:	iSMAC Key Partners:	SMArtCARE
1. Michelle Farrar (Australia) 2. Nathalie Goemans (Belgium) 3. Victoria Hodgkinson (Canada) 4. Jan Kirschner (Germany – Freiburg) 5. Vitaly Matyushenko (Ukraine) 6. Lindsay Murphy (UK/Ireland) 7. Damian Osredkar (Slovenia) 8. Miriam Rodriguez (New Zealand) 9. Laurent Servais (France) 10. Rasha el Sherif (Egypt) 11. Venkataraman Vishwanathan (India) 12. Maggie Walter (Germany – Munich)	1. Adrien Bretagne (Biogen) 2. Joanne Bullivant (UK, TGDOC) 3. Craig Campbell (Canada TGDOC) 4. Nathalie Goemans (Belgium, TGDOC) 5. Sue Hall (Biogen) 6. Victoria Hodgkinson (Canadian Registry) 7. Robert Hyde (Biogen) 8. Kirsten Konig (Freiburg Registry) 9. Joanne Lee (UK, TGDOC) 10. Anna Mayhew (UK, iSMAC) 11. Elena Mazzone (Italy, Physiotherapist) 12. Anne Oyewole (UK, TGDOC) 13. Aisha Rashid (Biogen) 14. Ray Su (Biogen) 15. Adrian Tassoni (Freiburg Registry)	1. Richard Finkel (US) 2. Eugenio Mercuri (Italy) 3. Francesco Muntoni (UK, London) 4. Volker Straub (UK, Newcastle)	Steering Committee: Jan Kirschner Günther Bernert Hanns Lochmüller Ulrike Schara Inge Schwersenz Maggie Walter SMArtCARE Team Freiburg: Kirsten König Adrian Tassoni Kristina Schachtrup Axel Gebert Astrid Pechmann David Schorling

Appendix B: Working Document (Feedback and Recommendations)

This document is provided as a separate supplementary document with this Workshop Report.

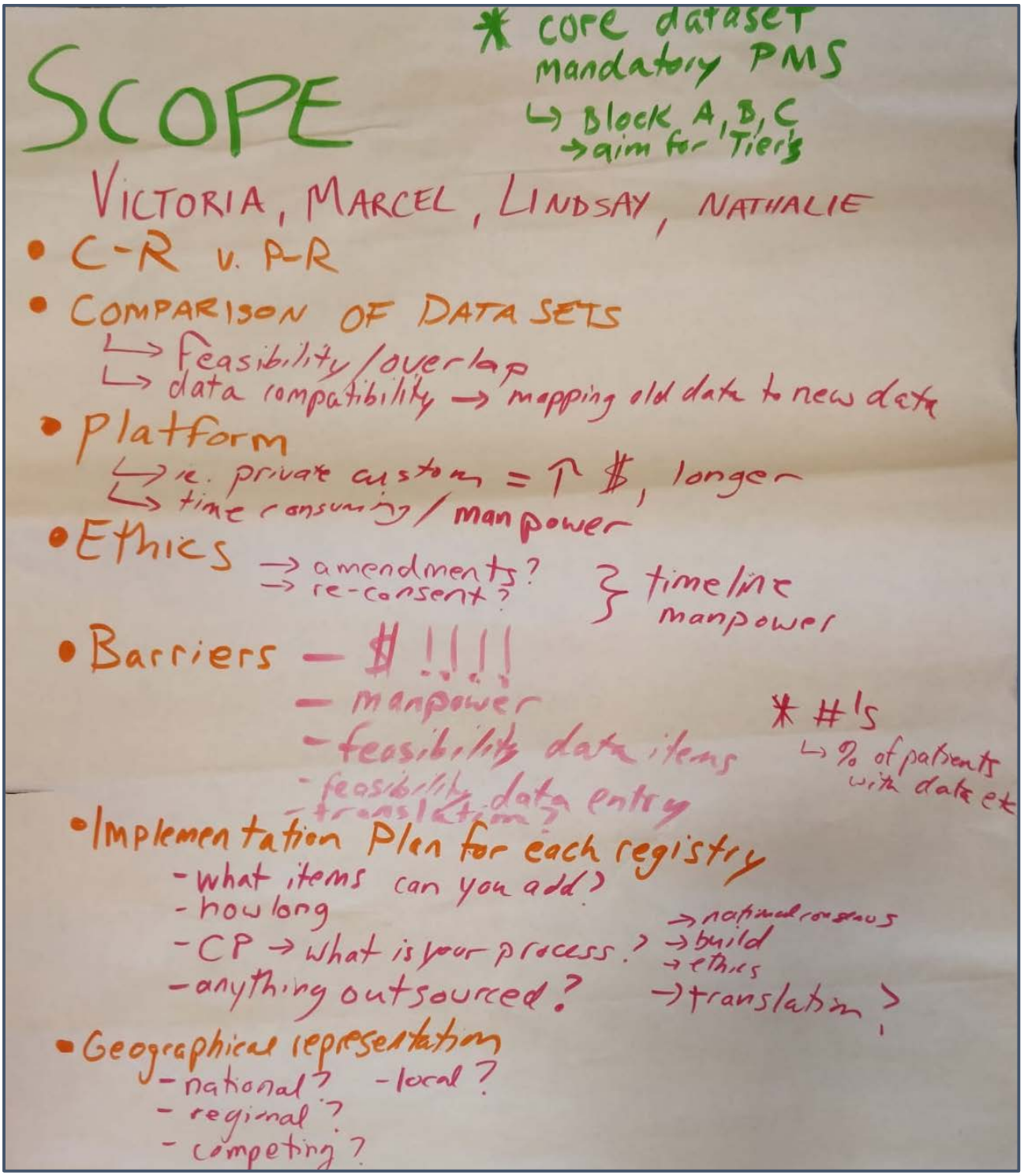
Appendix C: High-level Overview of Recommended Expanded Dataset

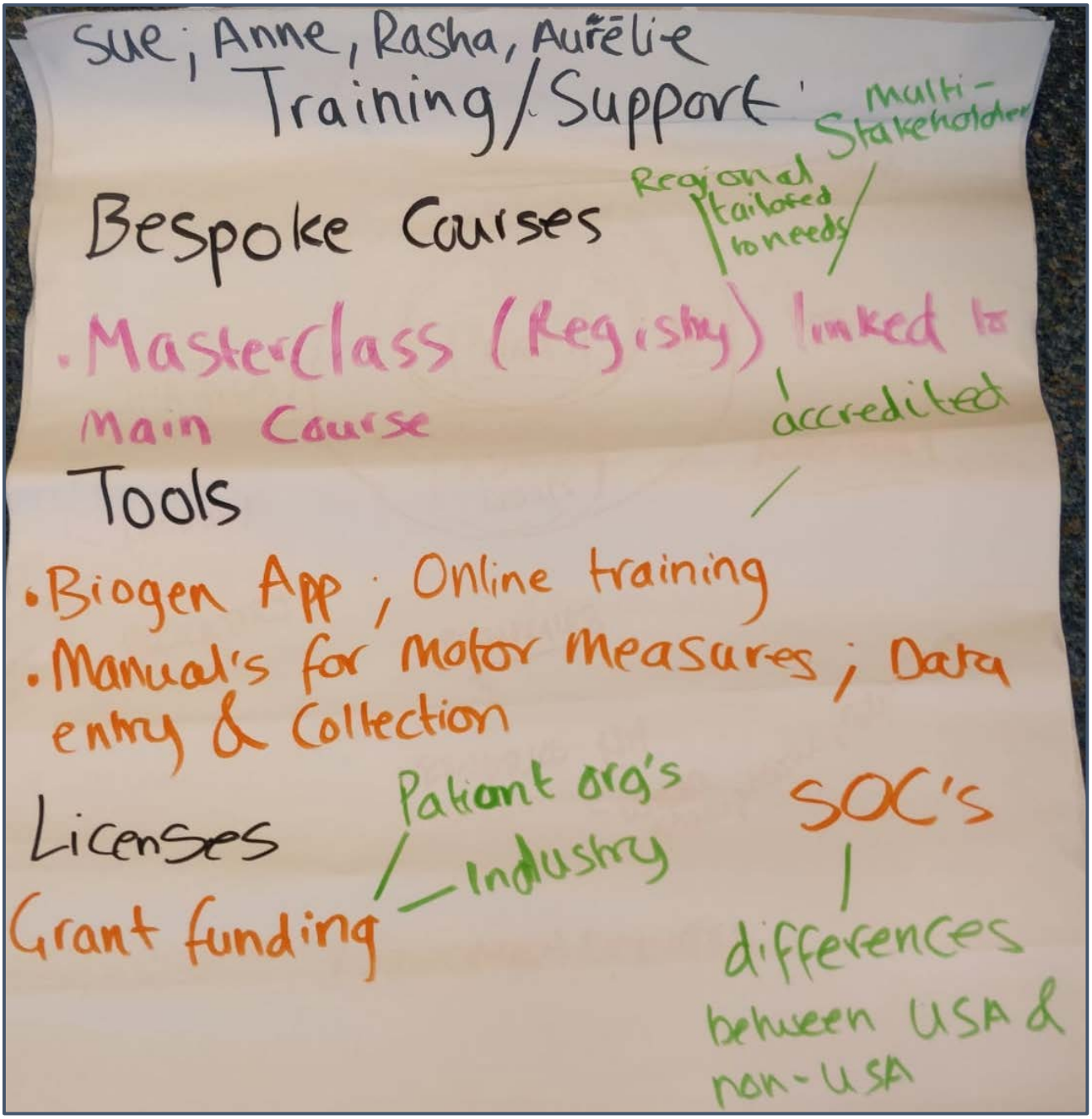
This document is provided as a separate supplementary document with this Workshop Report.

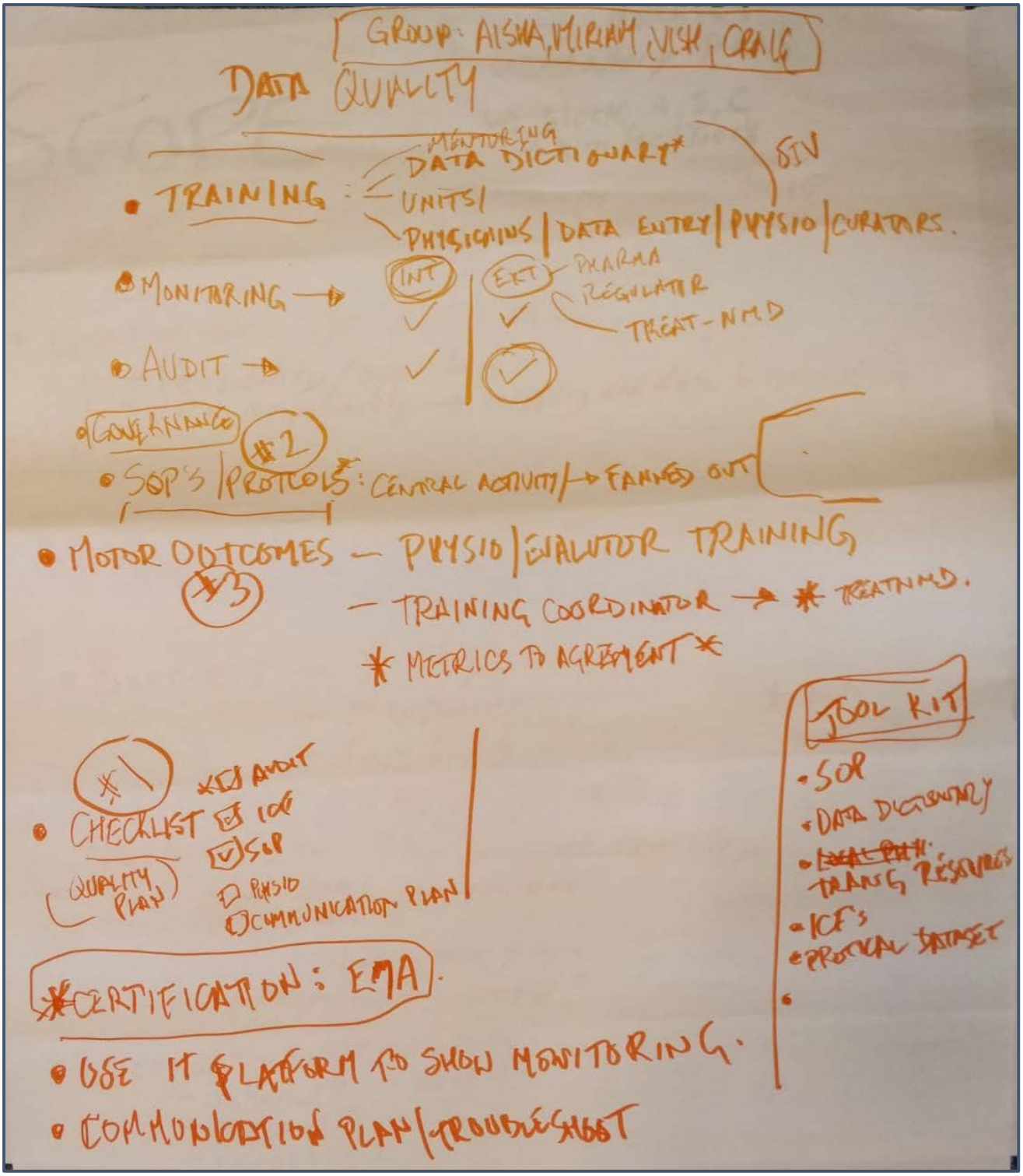
Appendix D: Full Recommended Expanded Dataset

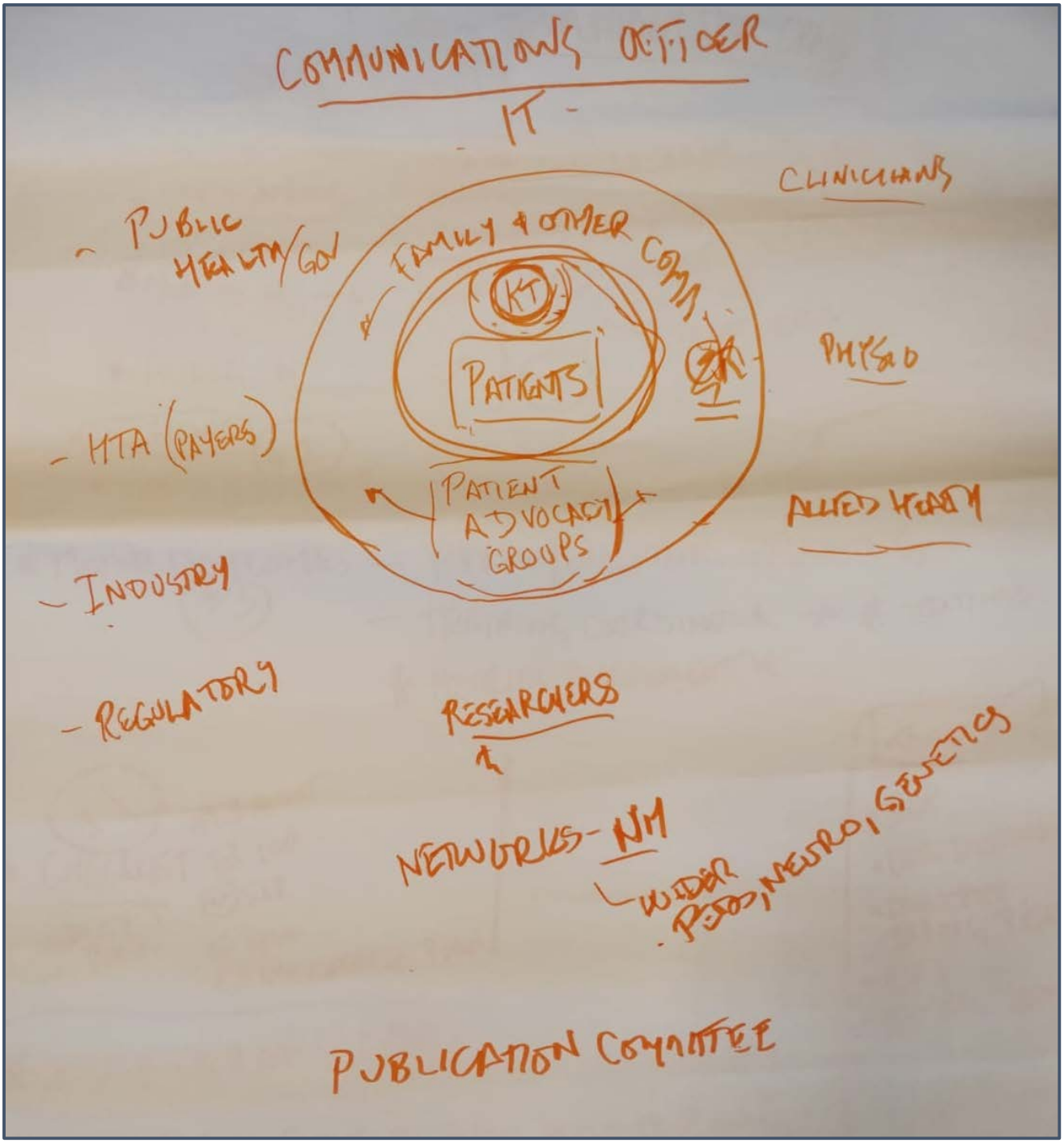
This document is provided as a separate supplementary document with this Workshop Report.

Appendix E: Implementation Planning Flipcharts




Sue; Anne, Rasha, Aurélie
Training/Support
Multi-Stakeholder
Bespoke Courses
Regional tailored to needs
• Masterclass (Registry) linked to accredited
Main Course
Tools
• Biogen App; Online training
• Manual's for Motor Measures; Data entry & Collection
Licenses
Grant funding
Patient org's
Industry
SOC's
differences between USA & non-USA


GROUP: AISHA, MIRIAM, VICKI, CRAIG
DATA QUALITY
TRAINING
MONITORING
DATA DICTIONARY*
UNITS/
PHYSICIANS | DATA ENTRY | PHYSIO | CURATORS.
SIV
MONITORING
AUDIT
INT
EXT
PHARMA
REGULATOR
TREAT-NMD
GOVERNANCE
#2
SOP'S | PROTOCOLS*: CENTRAL ACTIVITY → FANNED OUT
MOTOR OUTCOMES
#3
PHYSIO | EVALUTOR TRAINING
- TRAINING COORDINATOR → * TREATNMD.
* METRICS TO AGREEMENT *
#1
CHECKLIST
KEY ANALYT
ICF
SOP
PHYSIO
COMMUNICATION PLAN
QUALITY PLAN
TOOL KIT
SOP
DATA DICTIONARY
TRAING RESOURCES
ICF's
PROTOCAL DATASET
*CERTIFICATION: EMA.
USE IT PLATFORM TO SHOW MONITORING.
COMMUNICATION PLAN | TROUBLESHOOT


COMMUNICATIONS OFFICER
IT
CLINICIANS
PUBLIC HEALTH/GOV
FAMILY & OTHER CARERS
KT
PATIENTS
PHYSIO
HTA (PAYERS)
PATIENT ADVOCACY GROUPS
ALLIED HEALTH
INDUSTRY
REGULATORY
RESEARCHERS
NETWORKS - NM
WIDER PEDS, NEURO, GENETICS
PUBLICATION COMMITTEE