NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Data Collection Arrangement

Risdiplam for treating spinal muscular atrophy in children and adults [ID1631]

Company name: Roche Products Limited (the company)

Primary source(s) of data collection: Ongoing clinical studies FIREFISH and SUNFISH; SMA REACH; patient and carer quality of life data collection

Secondary source(s) of data collection: Ongoing clinical studies RAINBOWFISH and JEWELFISH

NICE Agreement Manager	Brad Groves, Associate Director, Managed Access
NHS England Agreement Manager	Fiona Marley - Head of Highly Specialised Commissioning
Roche Products Limited Agreement Manager	Karen Lightning-Jones - Head of Pricing, Reimbursement, Policy and Communications
SMA REACH Agreement Manager	Salma Samsuddin, SMA-REACH & UK (ISMAC) Trial Manager

1 Purpose of Data Collection Arrangement

1.1 The NICE Technology Appraisal (TA) committee has made a recommendation within the context of a Managed Access Agreement (MAA) for risdiplam for treating spinal muscular atrophy (SMA) in people 2 months and over, with a clinical diagnosis of SMA types 1, 2 or 3 or with pre-symptomatic SMA and one to four SMN2 copies (to be updated with TA/HST number after final guidance has been published).

1.2 The purpose of this Data Collection Arrangement (DCA) is to describe the key uncertainties identified by the committee, patient eligibility criteria, and the role and responsibilities to capture the data that could sufficiently address these uncertainties.

2 Commencement and period of agreement

2.1 This DCA shall take effect within 30 days after the publication of NICE Final Guidance.

2.2 Estimated dates for data collection, reporting and submission for NICE guidance update are:

End of data collection (clinical trials)	[redacted]
Data available for development of company submission	[redacted]
Anticipated company submission to NICE for guidance update	March 2024

2.3 The company anticipates the results from the additional data collected during the DCA period will be incorporated into an evidence submission and the corresponding economic model by March 2024.

2.4 The company will be responsible for:

- producing or commissioning the development of a data/statistical analysis plan to ensure methods and analytical outputs are clearly outlined and agreed within six months of publication of NICE Final Guidance.
- paying a proportionate share of the costs of data collection, validation and analysis
- providing a new evidence submission to NICE for this technology at the end of the data collection period
- adhering as closely as possible to the timelines presented in the document.
- informing NICE and NHSE&I in writing of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

- paying all associated charges for the guidance update. Further information is available on the NICE website.

2.5 Any changes to the terms or duration of any part of the DCA must be approved by NICE and NHSE&I.

2.6 NICE will, as far as is practicable, schedule the guidance update into the work programme to align with the estimated dates for the end of data collection. The guidance update will use the NICE process and methods in place at the time of the invitation to participate. For further details of the expected timelines for the NICE guidance update see the technology appraisal process guide.

2.7 If data collection is anticipated to conclude earlier than the estimated dates for data collection, for example due to earlier than anticipated reporting of an ongoing clinical trial, the company should note:

- Where capacity allows, NICE will explore options to reschedule the guidance update date to align with the earlier reporting timelines.
- It may be necessary to amend the content of the final real-world data report (for example if planned outputs will no longer provide meaningful data).

2.8 If data collection is anticipated to conclude later than the estimated dates for data collection, the company should note:

- The company must submit a written request to NICE and NHSE&I, with details of the extension requested, including an explanation of the factors contributing to the request.
- It may be necessary for the company to mitigate the impact of any delay, and reduce any risks of further delays.
- In the event of an extension, it may not be possible to amend the date of the final real-world data report, although NICE will explore options with NHR to provide data over the extended period.

2.9 If the company withdraws from the MAA or decides not to proceed with the NICE guidance update, they will still be required to make all new evidence available to NICE, NHSE&I and stakeholders for the purpose of an engagement event. The engagement event will involve a presentation with the new evidence and the implications for patient access, so that stakeholders can be informed of the proposed next steps and the factors contributing to this outcome. The presentations from this engagement event will be published on the NICE website.

2.10 If at the guidance update NICE publish negative final guidance for risdiplam, existing patients may continue to receive treatment until they and their treating clinician consider it appropriate to stop. The company and NHSE&I have agreed how access to treatment will continue in these circumstances: this is detailed within the commercial access agreement.

3 Monitoring arrangements

3.1 NICE will convene a Managed Access Oversight Group (MAOG) with representation from NICE, NHSE&I, the company, SMA REACH, SMA UK, Treat SMA, and Muscular Dystrophy UK.

3.2 The MAOG exists to oversee the operation of all aspects of the DCA and associated activity to ensure that the objectives of the agreement are met and that the data collection and analysis requested by the NICE committee is delivered on time for the guidance update at the end of the managed access period. The MAOG will regularly review progress with the implementation of the DCA and may recommend actions to address any issues that may arise, from time to time.

4 Patient Eligibility

4.1 Key patient eligibility criteria to start treatment within managed access include:

- Patient meets one of the following criteria:
    - Clinical diagnosis of SMA type 1, 2, or 3.

    - Pre-symptomatic of SMA and has been confirmed to have SMA via genetic testing and has one to four SMN2 copies.

- Risdiplam is used as a monotherapy.
- Must not have had successful treatment with onasemnogene abeparvovec. Non-successful treatment is defined in appendix A.
- No permanent ventilation (≥16 hours/day for 21 consecutive days in the absence of acute reversible infection)/ tracheostomy requirement at baseline. Patients who do not meet this criterion but otherwise meet the eligibility criteria should be discussed with the NHS England Clinical Panel.
- Mandated data items have been collected prior to starting treatment within this MAA (see section 7, Outcome data). Patients who have started treatment for SMA prior to this MAA are not required to repeat an assessment if a previous assessment has captured all mandated data items (see table 2) within the last 6 months.
- Patient/carer has signed the 'Managed Access Patient Agreement' and agreed to the associated monitoring, clinical assessments and sharing of data for the purpose of the MAA (see section 10, Patient consent).
- Clinician confirms they:
    - will submit data to SMA REACH as set out in the DCA.
    - have made the patient/carer aware that there are other treatments for SMA, which may be more suitable for that patient.
    - confirm annually, via completion of an addition Blueteq form, that the patient continues to receive benefit from treatment.
- Risdiplam will be otherwise used as set out in its Summary of Product Characteristics (SmPC).

4.2 If a patient meets any of the following stopping criteria the treating clinician should decide whether to terminate or continue treatment:

- the patient is diagnosed with an additional progressive life-limiting condition where treatment would not provide long- term benefit such as terminal cancer or catastrophic brain injury.
- the patient uses a different disease-modifying therapy to treat SMA.
- the patient/family/carer withdraws their consent or is unwilling to comply to the associated monitoring, clinical assessments or sharing of data for the purpose of the MAA.
- the patient is not receiving benefit from treatment, as confirmed either by the annual additional Blueteq form or by meeting any of the stopping criteria within Table 1, Endpoints, assessments and stopping rules.

Table 1. Endpoints, assessments and stopping rules

ENDPOINT	PROPOSED ASSESSMENT	STOPPING CRITERIA
MOTOR FUNCTION	Current Gross WHO motor milestone, including the appropriate scale as indicated by patient motor ability • HINE • RHS; • CHOP INTEND; • RULM Scale(s) will be chosen at baseline (prior to the initiation of therapy) based on the patient's motor function ability. Ideally the patient will remain on 1 scale for the length of the MAA however it is recognised that	**Where 1 scale has been measured from baseline**: total worsening in scale score corroborated by two consecutive measurements*. A scaled equivalent of these losses would apply if a domain was unmeasurable / not suitable** >2 points on horizontal kick or 1 point on other HINE scores excluding voluntary grasp >4 points on the CHOP INTEND scale >3 points on the RHS scale These scores are derived from the minimal clinical indicators of difference. **Where 2 (or more) scales have been measured from baseline:** total worsening in scale score(s) in the absence of any stability or improvement in other scales

	in some cases it is appropriate to capture a range of assessments and functional abilities (e.g. in type III ambulant patients). In the case of a change in the patient's clinical status then a final reading of one scale will be taken at the same time as a baseline for the next reading. The new scale will then be used for the patient's assessments.	corroborated by two consecutive measurements*. A scaled equivalent of these losses would apply if a domain was unmeasurable / not suitable** . For example, if a patient deteriorates on one scale (e.g. loses >3 points on the RHS scale) but maintains stability or demonstrates improvement on another scale that has been measured since baseline (e.g. RULM), **AND** in the opinion of the treating clinician the patient continues to receive clinical benefit from treatment then continuation of treatment may be considered. **These cases should be discussed with the NHS England Clinical Panel.** * in order to allow for confirmation of worsening and not an 'off' assessment day **if contractures develop or fracture occurs, then the unmeasurable domain of the scale is removed, and the delta change of remaining domains are scaled up to ensure the total achievable score of the scale remains.
VENTILATION REQUIREMENT	Patients, regardless of initially diagnosed motor milestone state, will be tracked for incidence, length and type of ventilation Rates of pneumonia	Permanent ventilation (≥16 hours/day for 21 consecutive days in the absence of acute reversible infection) or requirement of insertion of permanent tracheostomy. **Patients who meet this criterion should be discussed with the NHS England Clinical Panel.**
SURVIVAL	Patients, regardless of initially diagnosed motor milestone state, will be assessed for mortality with any cause and for mortality linked to SMA by ICD-10 coding relating to SMA in either death certificate PART I (including a, b and c) (immediate cause of death) or PART II (significant	All patients stop due to mortality

	conditions contributing to death) of death certificate	

4.3 Risdiplam has been available to patients in the United Kingdom via an Early Access to Medicines Scheme (EAMS). This has been open to patients with a confirmed diagnosis of type 1 or type 2 SMA who are not suitable for other currently available treatments. The Scheme opened in September 2020 and closed, following Marketing Authorisation, in July 2021. EAMS is closed to new patients; those enrolled on the EAMS will continue to be treated with risdiplam in line with the agreements between Roche and NHS Trusts.

4.4 As of October 2021, 207 people in England have received risdiplam via the EAMS. These early access patients, including those that do not meet the eligibility criteria, will be included as part of the DCA. Patients who do not meet the eligibility criteria will not have their data collection mandated.

4.5 The estimated patient numbers per year for this technology within the MAA period are:

As estimated by the company	Aligned with NICE Resource Impact Assessment team
As estimated by NICE Resource Impact Assessment team	Age 0-2 years Year 1: [redacted] Year 2: [redacted] Year 3: [redacted] Age 3-17 Year 1: [redacted] Year 2: [redacted] Year 3: [redacted] Adults Year 1: [redacted]

	Year 2: [redacted] Year 3: [redacted]

4.6 The eligibility criteria will apply to all patients during the managed access period including those currently receiving treatment within an Early Access to Medicines Scheme, compassionate use program, or those transferring from a clinical trial or from private treatment. Patients who do not meet the eligibility criteria to start treatment may continue without change to the funding arrangements in place for them before this MAA commenced.

4.7 NHSE&I will use an expert Clinical Panel, whose role will be to provide advice to treating centres on interpretation of the MAA criteria, including: starting and stopping criteria, and diagnosis.

4.8 After informed consent/assent is obtained, patients will undergo a screening up to 21 days prior to first dose administration, during which their eligibility for the MAA will be determined.

4.9 Treating clinicians must ensure that their patients are made aware of the eligibility criteria, stopping criteria, and any additional monitoring and clinical assessments required for receiving treatment within managed access.

5 Area(s) of clinical uncertainty

5.1 The NICE committee identified the following key areas of uncertainty:

- The suitability of the model for decision-making
- Long-term benefits with risdiplam are uncertain
- Methodological challenges and uncertainty associated with inclusion of caregiver utility values
- The approach to account for risdiplam's additional benefits that currently aren't captured in the clinical outcomes and economic model.

5.2 The committee expect further data collection will allow for a new model to be presented when the guidance is updated.

5.3 The committee concluded that further data collection within managed access could sufficiently resolve these uncertainties. For further details of the committee's discussion see section 3 of the Final Appraisal Document.

6 Source(s) of data collection

Primary and secondary sources of data collection

Primary source(s)	○ SUNFISH ○ FIREFISH ○ SMA REACH ○ Patient and carer quality of life
Secondary source(s)	○ RAINBOWFISH ○ JEWELFISH

Description of sources

6.1 FIREFISH and SUNFISH are primary sources of data collection; RAINBOWFISH and JEWELFISH are supportive secondary sources. FIREFISH and SUNFISH assess the safety and efficacy of risdiplam; FIREFISH in SMA 1 (infants; 1-7 months) and SUNFISH in SMA 2 and SMA 3 (children and young adults; 2-25 years). SUNFISH is a placebo controlled trial (2:1 risdiplam:placebo). RAINBOWFISH (<6 weeks old) assesses the safety and efficacy of risdiplam in infants with SMA who are not yet showing symptoms. JEWELFISH (children and adults; 6 months - 60 years) assesses the safety and tolerability of risdiplam in people who have previously received SMA treatments (pre-treated patients).

6.2 SMA REACH is a pre-existing disease specific database which collects data from all available SMA patients independent of their treatment regimen. SMA REACH collects data from routine clinical visits with data uploaded by a patient's healthcare team. It is hosted on the Certus platform and coordinated by the UCL Institute for Child Health.

6.3 The company is responsible for commissioning separate agreements to ensure that data is collected during the managed access period on patient and carer quality of life.

7 Outcome data

Clinical trials

7.1 The following outcome data will be collected through clinical trials during the data collection arrangement:

- Primary source: FIREFISH: primary endpoint - infants sitting without support for at least 5 seconds as measured by the BSID-III; secondary endpoints - motor function (BSID-III; HINE-2; CHOP-INTEND), survival, hospitalisations, bulbar function. Safety data including AEs and SAEs.

- Primary source: SUNFISH: primary endpoint - change from baseline in MFM32 score; secondary endpoints - motor function (RULM; HFMSE) and Patient Reported Outcomes (SMAIS - SMA Independence Scale). Safety data including AEs and SAEs

- Secondary source: JEWELFISH: primary endpoints - safety (incidence and severity of AEs, abnormal laboratory values, ECGs and vital signs), and tolerability and PK parameters, including mean plasma concentration, maximum concentration, area under the curve and minimum concentration of risdiplam and metabolites. Efficacy endpoints are exploratory endpoints

- Secondary source: RAINBOWFISH: primary endpoint - to evaluate the efficacy of risdiplam in infants with two SMN2 copies and CMAP amplitude ≥1.5 mV at baseline as determined by: • the proportion of infants sitting without support for 5 seconds after 12 months on treatment as assessed by the BSID-III Gross Motor scale. Secondary endpoints - proportion of infants developing clinically manifested SMA; time to death; time to death or permanent ventilation; proportion of infants alive; proportion of infants alive without permanent ventilation; motor function (BSID-III; CHOP-INTEND; HFMSE); change from baseline in growth measures; nutritional

status; change from baseline in CMAP amplitude; SMN protein and mRNA levels; PK and safety data

7.2 The FIREFISH and SUNFISH trials will provide long-term clinical effectiveness data of risdiplam, including:

- Survival, the attainment of motor milestones, a risdiplam specific treatment plateau, gains in upper limb function, changes in respiratory function, adverse events, utility values and treatment discontinuation.
- Such data are critical for informing an economic model for assessing the cost-effectiveness of risdiplam versus best supportive care.
- The JEWELFISH and RAINBOWFISH trials will also provide data on pre-treated and pre-symptomatic patients, respectively.

Data collected in clinical practice

7.3 SMA REACH UK will collect the following outcomes through its registry:

- patient & assessment details
- SMA type, including molecular genetic diagnosis
- cause of death in event of mortality
- nutritional status, including swallowing problems
- scoliosis
- motor function using SMA validated scales appropriate for the level of function of the patient (see below)
- fractures
- ventilation / respiratory events; respiratory function tests
- treatment use and outcomes, including reasons for treatment discontinuation

7.4 Several scales are used to measure motor function, the most appropriate scale is indicated by patient's motor ability. A scale will be chosen at initiation of therapy and measured at baseline. Ideally the patient will remain on that scale for the length of the MAA. If this is unfeasible due to change in the patient's clinical status, then a final reading of one scale will be taken at the same time as a baseline for the next reading. The new scale will then be used for the patient's assessment. The relevant scales are:

- World Health Organization (WHO) gross motor milestones will be collected for all patients.
- For patients <2 years of age who have not yet achieved independent walking, motor milestones will be assessed using Section 2 of the Hammersmith Infant Neurological Examination (HINE) and the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND).
- Patients who are ≥2 years of age but have not yet achieved the maximum score of 64 with CHOP INTEND will be assessed with both Revised Hammersmith Scale (RHS) and CHOP INTEND. The RHS should be performed after the CHOP INTEND with an approximately 15-minute rest period in between to allow the patient to be fully engaged with both assessments. Once a score of 64 is achieved, CHOP INTEND should no longer be assessed.
- All non-ambulatory patients ≥30 months of age will be evaluated using the Revised Upper Limb Measure (RULM). The RULM will continue to be performed should patients subsequently become ambulatory.

7.5 As part of its normal operations, SMA REACH collect a range of additional outcome data. These outcome data are not mandated as part of the DCA but may be included within interim and final reports.

7.6 Data will be collected or will continue for patients who:

- meet the stopping criteria and stop treatment
- choose to stop treatment or choose to use a different treatment for SMA

- currently receive treatment within the EAMS and are ineligible for treatment under the MAA. However, data collection for these patients is not mandatory.

7.7 The MAOG will regularly review progress with the data collection. The MAOG may amend the outcomes specified to be collected if it is determined that no meaningful data will be captured during the period of data collection.

7.8 Data collected through SMA REACH should be entered by the patient's healthcare team within a month of treatment commencing and after every routine 6 monthly follow-up clinic appointment. The patient consent form (see section 10, Patient consent) details the patient's assent to undertake the clinical assessments at these clinic appointments.

7.9 Any two entries need to be at least 4 months apart and a minimum of one data entry per patient per year is required to be captured after the initial assessment. Any missed clinic appointment for assessments should be rescheduled. If the patient has a worsening in any motor scale score the patient's next assessments must take place within the next 6 months.

Other data collection

7.10 During the period of the MAA the company is responsible for collecting further data that:

- describe patient's and caregivers' quality of life, physical functioning and other outcomes.

7.11 The company is responsible for exploring the most appropriate measures and outcomes that capture patient's and caregivers' quality of life.

7.12 The company is required to provide the MAOG assurance that these data will be collected during the managed access period. The company should provide details of the data collection for these outcomes to the MAOG for review within 6 months of publication of NICE Final Guidance.

Table 2: Outline of mandatory data items and clinical assessment schedule to be collected for patients

Data Item	Rationale for collection	Frequency			Data collection responsibility	Data collection tool / mechanism
		Baseline/ Pre-treatment	6-monthly	At event		
Patient identifier and treatment centre	Allows for linkage of patient to each registry record	x	x		Patient's healthcare team	SMA REACH
SMA type	Patient baseline characteristics	x	x			
Treatment dosage	Key treatment outcomes capture of those that stop treatment and those that switch treatment	x	x			
Concomitant therapies		x	x			
(Parental) perceived benefit			x			
Reason for any treatment discontinuation		x	x			
Mortality and cause of death	Key survival outcome			x		
WHO MOTOR ACHIEVEMENT	Key motor function outcomes	x	x			
RULM*		x	x			

RHS*	Required for stopping criteria *The most appropriate scale is indicated by patient's motor ability	x	x			
HINE*		x	x			
CHOP-INTEND*		x	x			
summary of contractures	health-related problem due to SMA May prohibit measurement of motor milestones	x	x		Patient's physiotherapist	
Presence and magnitude of scoliosis	Key health-related problem due to SMA May impact delivery of specific SMA treatments	x	x		Patient's healthcare team	
Use of thoraco-lumbo-sacral orthosis (TLSO) brace		x	x			
Scoliosis surgery, date and type		x	x			
Fractures	health-related problem due to SMA May prohibit measurement of motor milestones	x	x			
Forced vital capacity		x	x			

peak cough velocity	Key ventilation / respiratory outcomes	x	x			
type of ventilation used		x	x			
estimation of hours of ventilation		x	x			
Chest infections per year		x	x			
Nutrition status, including swallowing problems	Resource use / nutritional status outcomes	x	x			
nasogastric tube use		x	x			
gastrostomy placement		x	x			
Patient quality of life measures	Key uncertainty	-	-	-	To be confirmed	To be confirmed

8 Analyses and Reports

Clinical trials

8.1 The detailed Statistical Analysis Plans for all four risdiplam trials have been made available to NICE and the MAOG, in confidence.

8.2 For each of the four clinical trials for risdiplam, yearly interim analyses are planned. See section 8.3 for an overview.

8.3 Below is a table outlining the planned interim and final analysis timelines including Clinical Cut Off Date, the availability of outputs and Clinical Study Report availability. The data availability for SUNFISH and FIREFISH as primary sources have determined the end of data collection as indicated in section 1.

All data will be reported in the final CSRs (5-year) for each study. The interim data cuts (e.g. 3-year, 4-year) may only contain a subset of data. This will be decided on an "as required" basis. The rationale for this is because no CSRs are planned for these data cuts. Pooled safety analyses can be made available each year.

Study	**Reporting**	**CCOD**	**Outputs**	**CSR**
SUNFISH (Part 1 and Part 2 separate)	3-year	[redacted]	[redacted]	No
	4-year	[redacted]	[redacted]	No
	5-year	[redacted]	[redacted]	Yes (Final)

FIREFISH (Pooled Part 1 and Part 2, also separate if needed)	3-year	[redacted]	[redacted]	No
	4-year	[redacted]	[redacted]	No
	5-year	[redacted]	[redacted]	Yes (Final)
JEWELFISH	2-year	[redacted]	[redacted]	Yes
	3-year	[redacted]	[redacted]	No
	4-year	[redacted]	[redacted]	No
	5-year	[redacted]	[redacted]	Yes (final)
RAINBOWFISH	1-year	[redacted]	[redacted]	Yes
	2-year	[redacted]	[redacted]	No
	3-year	[redacted]	[redacted]	No
	4-year	[redacted]	[redacted]	No
	5-year	[redacted]	[redacted]	Yes (final)

Data collected in clinical practice

8.4 The company is responsible for producing or commissioning development of a detailed data/statistical analysis plan within 6 months of publication of NICE Final Guidance, for review by the MAOG. This will detail the analyses that will

be presented within the interim and final reports, the methodologies used, and the schedule of delivery.

8.5 The company, in partnership with NICE and SMA REACH will be responsible for developing the data analysis plan.

8.6 SMA REACH will be responsible for analysing the data collected within clinical practice and producing the corresponding reports.

8.7 Subgroup analyses planned to be undertaken will be detailed within the data analysis plan. However, at a minimum data will subsequently be analysed separately at the point that patients:

- meet the stopping criteria and stop treatment
- choose to stop treatment with risdiplam or choose to use a different treatment
- For all patients within the EAMS that are ineligible for treatment under the MAA. However, data collection for these patients is not mandatory.

8.8 At a minimum the number of patients starting treatment will be shared at each MAOG meeting to monitor the uptake in clinical practice and confirm that patients are being captured within SMA REACH.

8.9 The reports produced will include anonymised summary data, with the raw data also supplied to NHSE&I and NICE upon request. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk.

8.10 At the end of the data collection period a final report will be produced and shared with all members of the MAOG in advance of the NICE update of guidance. Data and analyses contained within the final report will be available to all member of the MAOG to use as part of an evidence submission to NICE as part of the guidance update.

8.11 The final report will also form part of NHSE&I's submission to the guidance update. The final report will therefore be publicly available during the guidance update.

8.12 The availability of the final report will be aligned to the availability of data from the other primary sources. The data collection in clinical practice will end at a date that will allow for the upload of data, data cleaning, data analysis, and report production.

Other data collection

8.13 For data collection related to patient and carer quality of life the company is responsible for producing or commissioning development of a detailed data/statistical analysis plan within 6 months of publication of NICE Final Guidance, for review by the MAOG. This will detail the analyses related that will be presented within interim and final reports, the methodologies used, and the schedule of delivery.

9 Ownership of the data and governance arrangements

Clinical trials

9.1 For all clinical trial data listed above, Roche Products Limited will be the owner

9.2 Roche Products Limited will be responsible for ensuring they have permission to share the clinical study report, including non-patient identifiable data and analyses as part of their submission for the guidance update.

Data collected in clinical practice

9.3 The clinical data collected in clinical practice will be owned and processed by the SMA REACH, and shared by prior agreement with the company, NHSE&I and NICE. The lawfulness of this processing and sharing is covered under article 6(1)a of the United Kingdom General Data Protection Regulations (GDPR) (the data subject has given consent to the processing of his or her

personal data for one or more specific purposes; see section 10, Patient consent). The data use will be governed by data privacy laws. SMA REACH has governance structure to ensure correct use of the information. The data can also be repurposed for other research questions subject to appropriate ethical and legal checks provided these have been consented for by MAA participants.

Other data collection

9.4 For data collection related to patient and carer quality of life the company is required to provide the MAOG assurance that the governance arrangements have been established to allow analysis and submission of data as part of the NICE guidance update. The relevant terms of these agreements should be presented to the MAOG for review within 6 months of publication of NICE Final Guidance.

10 Patient consent

10.1 To receive treatment, patients or their guardians and clinician must sign up to the 'Managed Access Patient Agreement' included in Appendix B to this DCA. The agreement details the patient/carer:

- Understands the eligibility criteria, including the eligibility criteria, stopping criteria, and the requirement to attend the routine 6 monthly follow-up clinic appointments for assessments
- Agrees for the treating clinician to enter collected data to the SMA REACH registry
- Agree to co-operate with the treating centre to ensure that they/their child receives the standard of care as indicated by the status of their/their child's condition.

10.2 SMA REACH requires a separate consent form to be completed. This form details:

- that clinical information will be collected and saved in the SMA REACH UK database

- that relevant sections of any medical notes and data collected during the study may be looked at by employees from Regulatory Authorities or from Great Ormond Street Hospital/ Institute of Child Health (and other academic institutions), for monitoring and auditing purposes

- If enrolled onto the MAA pseudonoymised personal data will be collected and saved in the SMA REACH UK. This will be shared with NHSE&I, NICE, and the company

- Additional optional assessments. These additional assessments are not mandated as part of the DCA.

11 Funding for data collection and analysis

11.1 The company will be required to pay direct and associated costs for:

- Collection and entry of data into the specified databases,

- Database management – including data processing and quality assurance,

- All costs related to the production of interim and final analyses and reports,

- Costs associated with accessing and linking data to other sources (if applicable),

- Any other costs identified that are relevant to data collection and analysis associated with the uncertainties identified by the NICE committee.

11.2 The company is responsible for agreeing and documenting a separate agreement concerning the above direct and associated costs.

11.3 The company is required to provide the MAOG assurance that all separate agreements concerning the above direct and associated costs have been agreed. The relevant terms of these agreements should be presented to the MAOG for review within 6 months of publication of NICE Final Guidance.

12 Patient Safety

12.1 The company, NHSE&I, and clinical MAOG members, have the responsibility to monitor the safety profile of the technology and must provide an overview of any new or updated safety concerns to MAOG. If any new safety concerns are confirmed, NICE and NHSE&I will take steps, as appropriate, to mitigate the risk including but not limited to updating the eligibility criteria or recommending that the managed access agreement be suspended.

13 Publications relating to the DCA

13.1 The publication of any data collected within NHS clinical practice as part of this DCA is not permitted without the permission of the MAOG until after the final report has been published on the NICE website as part of the guidance update. This may include publication in a peer reviewed journal, presentations, information leaflets, or any publicly available site.

13.2 Publications regarding the implementation or managed access process may be permitted as long as no data collected in clinical practice is included (e.g. patient leaflets, NICE presentations about operational aspects of MAAs).

13.3 Additionally, before proceeding with the development of a publication any draft abstracts or manuscripts related to this DCA must be shared with the MAOG prior to submission at conferences, in journals or any other publicly available site.

13.4 The contribution of all relevant individuals involved must be acknowledged in any publications related to this DCA. Authors will need to contact the NICE Managed Access Team for the full list of relevant individuals.

14 Data protection

14.1 Patient data collected as part of this Data Collection Arrangement will be managed in accordance with all applicable data protection legislation, including but not limited to the Data Protection Act 2018 and the UK General Data Protection Regulation.

14.2 The terms of the Managed Access Agreement relating to data protection, as apply between NHSE&I and the company, shall also apply between the parties to this Data Collection Arrangement in relation to the performance of their obligations under this Data Collection Arrangement.

15 Equality considerations

15.1 Do you think there are any equality issues raised in data collection?

☐ Yes ☒ No

16 List of abbreviations

Abbreviation	Definition
AE	Adverse event
BSID-III	Bayley Scales of Infant and Toddler Development
CHOP-INTEND	Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders
DCA	Data Collection Arrangement
EAMS	Early Access to Medicines Scheme
EAP	Expanded Access Programme
FAD	Final appraisal document
HINE	Hammersmith Infant Neurological Exam
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
MAA	Managed access agreement
MAOG	Managed Access Oversight Group
NICE	National Institute for Health and Care Excellence
NHS	National Health Service
NHSE&I	NHS England and NHS Improvement
RHS	Revised Hammersmith Scale
RULM	Revised upper limb module
SAE	Serious Adverse Event
SMA	Spinal muscular atrophy
SUSAR	Suspected unexpected serious adverse reactions
SmPC	Summary of Product Characteristics

TA	Technology Appraisal
GDPR	United Kingdom General Data Protection Regulations
WHO	World Health Organization

17 Version control table

Version	Date	Description of changes/purpose
1.0	November 2021	Release of Final Appraisal Document and DCA