NICE Methods Review Consultation Response

1. Methods: Valuing the benefits of health technologies

How strongly do you agree or disagree with the proposals related to:

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Don't know / NA
A modifier for severity of disease			x			
Consideration of uncertainty in decision making		X				
Health inequalities			x			
Aligning modifiers across programmes		x				
Discounting				X		

Of the 2 alternative options presented in proposal g and h, which do you prefer:

Option 1 x
Option 2

A modifier for severity of disease

Please use this space to share any comments on the options:

We welcome the introduction of a severity modifier to replace the 'end of life' modifier as it will cover a broader range of conditions. However, we understand that NICE has based its proposals on a retrospective count of topics that qualified for the end-of-life modifier and focused on cost neutrality. As a result, we understand that only a very small number of treatments would be eligible for the higher QALY rating which is at most a £50,000 threshold for the most severe conditions. This maintains the wide gap between the £100,000 ICER for the HST compared to those following the STA route which is an issue we have consistently raised as of concern.

Treatments for patient populations such as **all** those who have the rare condition 5q SMA will continue to be channelled down the STA route. This has proved to be very challenging in recent years for two treatments for what is acknowledged to be a complex muscle wasting condition which impacts increasingly severely over time. We have seen both pharmaceutical and ERG economists grappling with modelling in an endeavour to meet STA thresholds. The time and money this has taken has been immense to say nothing of the pain of the SMA community waiting for outcomes and the difficulties the committees have faced with their decision making.

Though neither option appears to meet the ambition of opening up access to innovative treatments for patients with a wider range of conditions and closing this HST/STA gap, Option 1 with a higher top threshold modifier is the better current option. We are pleased to see this first step and look forward to hearing more about the further work that will follow on this.

Consideration of uncertainty within decision-making

We welcome NICE's recognition of the importance of a more flexible approach to uncertainty where a condition is rare, impacts on children and where the technology is innovative. SMA, a rare condition which, in the majority of cases, impacts on children, and the three innovative new technologies with limited longer term trial data – zolgenmsa (HST), nusinersen (STA), and risdiplam (STA) – are examples. Clinical and cost effectiveness uncertainty have been at the heart of these appraisals leading to lengthy appraisals, in particular for nusinersen. We have seen pharmaceutical and ERG economists grappling with modelling in an endeavour to address uncertainties and meet STA thresholds. The time and money this has taken has been immense to say nothing of the pain of the SMA community waiting for outcomes. The need for flexibility and difficulties of the committees enabling these treatments to cross the line within current constraints has been evident. However, we are also very aware that flexibility can in itself bring uncertainty and inequality. How it is used and why needs to be transparent to all stakeholders We hope that the learning from these SMA appraisals will be taken into account when considering how this will be taken forward.

Health inequalities

This remains an important principle and all possible causes should be considered in all appraisals. As well as being faced with the daily social barriers to inclusion, people living with rare diseases such as SMA experience difficulties in accessing levels of health and social care that allow them to live the best quality of life possible.

Discounting

Gene therapies such as zolgensma for SMA are one of the most potentially transformative, and other treatments for SMA are also changing lives in ways that will have long term positive outcomes. The voluntary and statutory pricing arrangements in place provide financial certainty on government spending levels and place the risk of overspend on the pharmaceutical industry. We are therefore disappointed to read that though NICE accepts the case for the introduction of a 1.5% discount rate for cost and health effects which recognise and value the effectiveness of a treatment which bring long term benefits, there will be no immediate change. We hope there will be action on this at the earliest possible time.

2. Methods: Understanding and improving the evidence base

How strongly do you agree or disagree that you support proposals related to:

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Don't know / NA
Implementing the proposed cases for change for sourcing, synthesising and presenting evidence and considering health-related quality of life		x				
Considering real-world evidence		x				
Calculating the costs of introducing health technologies			x			
Analysing uncertainty		x				

Health -related quality of life

We are currently part of a working group of clinicians and patient representatives looking at PROMS for people who have SMA. It has been evident that there is much more work to be done to find measures that will capture what health-related outcomes have meaning for people who have SMA in their day to day lives. We welcome NICE's commitment to provide additional guidance and flexibilities as to what measures it will accept and look forward to a positive response from NICE to the recommendations that this working group makes.

The impact of SMA on carers and how to capture this has been the subject of many surveys and much debate as we have journeyed through the three treatment appraisals. This has added to the delays in the process. We agree that much more work on consistent measuring and valuing of carer health-related quality of life is needed - as outlined in CMAC's response.

Considering real-world evidence

Real world evidence is extremely important for rare diseases such as SMA. Now there are treatments, full randomised controlled trials of new technologies are simply unethical. We have seen many countries introduce access to new SMA treatments more quickly than the UK and their experience provides invaluable insight into their clinical effectiveness. The importance of patient reported outcomes and the impact of a treatment on someone's day-to-day life can often be best captured in videos and testimonials as we saw when access to nusinersen for SMA Type 3 was reviewed We welcome NICE's commitment that it will not place any restrictions on the types of evidence that it will accept and look forward to hearing more about this.

Calculating the costs of introducing health technologies

Though we understand the overall need for this, we are concerned by the proposal not to recommend a treatment for a subgroup for which the treatment is not cost effective, even when the treatment is found to be clinically and cost effective for the whole population.

We have seen the use of subgroups with 5q SMA and nusinersen. Decision making was based on subgroups of 'type' of 5q SMA. This is despite 5q SMA is a spectrum with no clear dividing line between types, and despite the fact that the underlying cause for all with the condition is the same as is the appropriateness of the biology of the treatment mechanism. The decision to exclude a subgroup from treatment had a massively detrimental impact on the people who were denied access to treatment – not only did their muscle wasting condition progress but they also suffered great emotional harm. We acknowledge the reason for the exclusion was due to lack of clinical trial and cost effectiveness evidence for this particular subgroup at the time of the initial appraisal and that NICE was exceptionally able to address this inequality when it agreed to keep the door open and assessed new evidence.

NICE's proposals to widen its evidence base from the outset will help to ensure there is no repeat of these circumstances, but we suggest the use of subgroups in 5q SMA in this way should serve as a sharp check on future consideration of such mechanisms for other conditions and treatments.

Technical Engagement

Having been involved in this stage of the appraisal process we are very supportive of this step remaining as standard. It enabled more relaxed wide-ranging discussions than can take place

at a committee meeting and is especially important for patient experts who may be more daunted by the more formal public setting.

Managing high company base case ICERs

We have seen high company base case ICERs as the norm with SMA treatments, that fortunately have progressed, and the importance of the patient and clinical voice throughout the next stages. This has informed discussion of the potential transformative impact of a treatment and the reality of the impact of the condition and unmet need based on knowledge that the company/NICE cannot be expected to possess in the same way. We consider it essential that these voices are heard at this earlier stage and the process and decision making is open and transparent to all.

Alternative draft scope consultation timings

Though we support NICE's desire to speed up timeframes for draft scopes and appraisals of new treatments, having been caught in the protracted discussion around nusinersen, the size and capacity of patient groups can make it extremely challenging to respond in an informed way at the best of times. We suggest that reviews of timelines consider the impact this may have on patient participation and what measures NICE can put in place to support patient groups – such as assistance to set up, administer and collate results from patient population surveys.

3. Processes: Commercial and Managed Access

Managed access activity

We welcome confirmation that all committees will be able to make a recommendation for managed access and the commitment to develop a single approach to support streamlined assessment at the end of a period of managed access.

We have been pleased to be invited to and part of MAA proposal and oversight discussions and observe a positive attitude to patient participation.

Though outside the scope of this consultation we do wish to highlight the importance of timely access to treatment once an MAA has been agreed. Our experience with the nusinersen SMA MAA is that it has not become a timely reality for many adults who have faced a roller coaster of emotion hearing they are eligible for treatment but then finding that the Trust(s) that supposedly will deliver are not ready to do so. The importance of clear timely communication with the patient community at all stages so that expectations are managed cannot be stressed enough. Though timely funding and covid have been factors that have impacted on delivery, this failure appears to be in part due to a contract process that allows a Trust to tender for and accept a contract before there is a business plan and robust demonstration of an ability and management willingness to actually provide the service. More than two years on from NICE's MAA patients and clinicians have been badly let down by one Trust in particular where there is still no actual service delivery.

We have been pleased to be involved in a very small way with the IMPACT HTA group that has been conducting a wide best practice review of MAAs including how best to involve Patient Groups in the assessment processes. We look forward to NICE adopting their advice.

4. Topic Selection: Highly specialised technologies

How clear or unclear is the aim of the HST evaluation programme?

	Very clear	Clear	Neutral	Not very clear	Not clear at all	Don't know / NA
The aim of the HST evaluation programme is:		x				

How clear or unclear is the refined routing of the HST evaluation programme?

	Very clear	Clear	Neutral	Not very clear	Not clear at all	Don't know / NA
The routing criteria for HST is:				x		

Please use this space to share any comments on the proposals on the routing criteria for HST:

We welcome NICE's efforts to make the criteria for an HST simpler and more transparent. In particular we welcome the clarity of a 'very rare' population-based criteria of a prevalence of 1: 50,000 (1,100 people in England). Our experience with SMA, however, has shown how staggeringly unable we have been to say how many people there actually are living with this condition. There is a great need to improve the use of national health condition registries to enable us to monitor population health and treatment outcomes

We do have concerns about the impacts of the following additional population-based aspects of the new criteria and what we understand their impact will be:

- a treatment population of 300 for its licensed indication and no more than 500 across all its indications. There is reference to flexibility for populations greater than 300 based on severity of the disease, lack of effective treatments and potential for significant benefit from treatment that would be gathered via scoping. However we don't know what this will look like in reality.

- for one off treatments generally a small prevalent population of up to 50 patients and an incidence of no more than 40 patients a year

We are concerned about the impact that both these new rules could have on transformative treatments for SMA and no doubt others. Zolgensma, a 'one off' gene therapy is a case in point.

In view of current trial evidence, zolgensma is only funded for those who have SMA Type 1 though its licence would allow for wider use and further evidence that could satisfy NICE's new openness could be accepted in due course and therefore increase the prevalent

numbers. Additionally there is likely to be new evidence of its suitability for another wider group - via newborn screening. The combination of these two very positive developments that would transform the lives of children affected by this severe condition would result in a short-term

increase in numbers likely to make it out of scope for an HST and plunge it into the wide HST / STA ICER threshold gap that will remain.

On the one hand we are celebrating the development of the gene therapy and encouraging further development of this ground-breaking technique. On the other we are restricting the numbers that may be treated each year.

Similarly if this treatment were to be developed further and could address others in the whole prevalent population, it would face the STA barriers. Perversely the system therefore sets up a disincentive to investment in innovation and change.

We suggest there is further discussion and review of these two new criteria.

How clear or unclear is the eligibility criteria for devices, diagnostics and digital technologies?

	Very clear	Clear	Neutral	Not very clear	Not clear at all	Don't know / NA
The eligibility criteria for devices, diagnostics and digital technologies is						x

13th October 2021