National Institute for Health and Care Excellence

IP1877 Electrical stimulation of the pharynx for neurogenic dysphagia

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Comments disagreeing with draft recommendations 1.1 to 1.3				
1	Consultee1 NHS Professional	**n/a**	Our trust has used the Phageynx treatment trial pack to treat 4 stroke patients. All 4 of these patients had successful outcomes with Phagenyx. They experienced extensive periods (up to 95 days) of severe dysphagia which required them to be nil by mouth or them only being safe to swallow minimal oral intake (still requiring enteral feeding). No other dysphagia treatment was working. All these patients were able to commence oral intake within 2 weeks of starting Phagenyx treatment. We have found that Phagenyx is a beneficial treatment for neurogenic dysphagia of a sensory nature (i.e., the patients would be at risk of silent aspiration). There are currently very limited therapy options for these patients. From clinical experience, these patients are therefore notoriously difficult to treat and often have persisting dysphagia. We would therefore hypothesise that this is a treatment option for stroke patients, that have a sensory element to their dysphagia, rather than a solely motor dysphagia. After the successful trial pack, Phagenyx was taken to our Trust's New Techniques & Medical Devices panel. The current draft NICE guidance was discussed in this panel, and secondary to the current guidance, we were advised that we either must re-visit the panel when/if NICE guidance approve the use of the device, or only use within a research project. We are currently exploring whether research can be facilitated but this is likely to be difficult alongside full time clinical duties. This has a significant impact on our clinical practice, and means that we will have patients that miss out on a treatment option, where there is a low risk (as identified by NICE) to substantial potential benefit.	Thank you for your comments. The consultee reports anecdotal success with the procedure in people with neurogenic dysphagia with a sensory element after stroke. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4. The committee acknowledged that treatment options are limited in the section of the guidance called 'Why the committee made these recommendations'. The consultee believes a more clinically relevant subgroup for this recommendation would be 'stroke patients with a sensory element to their dysphagia'. The committee considered this comment but decided not to change the subgroup defined in the 'special arrangements' recommendation. The rationale is detailed in the section of the guidance called

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			When presenting to our New Techniques & Medical Devices panel, we also noted that for non-tracheostomised stroke patients, 2 systematic reviews were included. The Cheung systematic review, which only included stroke patients, did find a moderate effect size compared to sham treatment. The Speyer (2022) systematic review found no statistical difference between groups. However this was non stroke specific, e.g. including MS patients. We question whether this systematic review should be included if the advice from NICE is for stroke patients only?"	'Why the committee made these recommendations'. The Cheng (2022) systematic review was included in the evidence and was considered by the committee, but concerns were raised about the validity of the meta-analysis of PES outcomes. The Speyer (2021) meta-analysis was included in the evidence and considered by committee because the remit of the topic title is 'neurogenic dysphagia' which includes people with MS.
2	Consultee 2 NHS professional	1.1	Neurogenic dysphagia occurs in stroke populations and tracheostomy populations. These do not need to co-occur for pharyngeal electrical stimulation to be beneficial.	Thank you for your comment. The committee considered this comment but decided not to change the subgroup defined in the 'special arrangements' recommendation. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'.
3	Consultee 2 NHS professional	Why the committee made these recommendations	For people with neurogenic dysphagia, primarily those with reduced laryngopharyngeal sensation as a result of stroke OR prolonged invasive mechanic ventilation via ETT or tracheostomy with cuff up, this procedure should only be used with special arrangements.	Thank you for your comment. The committee considered this comment but decided not to change the subgroup defined in the 'special arrangements' recommendation. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'.
4	Consultee 2 NHS professional	Why the committee made these recommendations/ 1.1	there is a wealth of anecdotal evidence to support the use of pharyngeal electrical stimulation with patients post stroke (who do not have a tracheostomy) and for those who have a tracheostomy but have not had a stroke.	Thank you for your comment. The committee can only consider published evidence in their assessment of clinical efficacy.

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				Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.
5	Consultee 3 NHS professional	**n/a**	I have observed a variety of stroke patients benefit from this therapeutic tool, both those with and without a trache. These patients without a trache can still experience severe sensory pharyngeal dysphagia which can greatly limit their ability to manage any level of oral intake safely. With this limitation I have been able to observe their desire to have something to eat/drink however the risk to their health prevents this from happening. There are not many therapeutic options for patients with a sensory dysphagia, and PES has opened By carrying out PES treatment these patients have been able to progress onto a level of oral intake which has been able to give them some pleasure whilst they are struggling with their other impairments. This is a safe treatment that has been in clinical circulation with a variety of populations for over 10 years with no serious adverse events to report. Over this time the benefits have greatly outweighed the cost of the treatment. One important factor to note is the reduction in length of stay both within critical care settings but also acute ward settings. My Trust has been able to use PES for the past few months and we have been amazed at the opportunities this opens up for our patients. We hope to gain our own PES to use for the foreseeable future and continue to benefit our patients.	Thank you for your comment. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by committee. This has been noted in section 3.4. The committee considered this comment but decided not to change the subgroup defined in the ‘special arrangements’ recommendation. The rationale is detailed in the section of the guidance called ‘Why the committee made these recommendations’. The committee acknowledged that treatment options are limited in the section of the guidance called ’Why the committee made these recommendations’.

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6	Consultee 4 NHS professional	**1.1**	Why are 'special arrangements' needed for this when it is used in many other countries and is researched for a number of patient conditions, not just stroke patients with a t-tube. In our trial use we have reviewed all the risk factors and had discussions with the relevant consultant/ patient and others involved in patient care about the risks, safety guidelines and procedure before we have used it with non tracheostomised stroke and non-stroke patients, with very good results. It is also currently one of few treatments available for patients with a sensory element to their dysphagia, so should be available for all those patients assessed to be suitable by a trained Speech & Language therapist and have no contraindications against the treatment	Thank you for your comments. When making their decision, the committee considered recommendations from other guidelines, which were presented in the overview. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4. The committee acknowledged that treatment options are limited in the 'Why the committee made these recommendations' section of the guidance.
7	Consultee 4 NHS professional	1.2	Why do we need to inform the clinical governance lead if this is a recognized clinical treatment for a specific patient type. As speech & language therapists we are a recognized independent clinical profession who are led at all times by HCPC and RCSLT standards, so not sure why a Trust clinical governance led would need to be involved as we all commit to maintaining and reviewing our own clinical competence in all clinical interventions	Thank you for your comments. The consultee reports that the intervention is delivered by speech and language therapists, who have independent governance and standards. The section of the guidance called 'Why the committee made these recommendations' explains that the special arrangements recommendation has been made because of uncertainty about the efficacy of the

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				procedure. This recommendation encourages the additional research that is needed to reduce uncertainty about the efficacy of this procedure. Informing the clinical governance lead is a standard part of a special arrangements' recommendation, in order for organisations to support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
8	Consultee 5 Phagenesis Ltd	**1.1**	Company response with respect to the wording of the guidance and proposed scope of use: The company appreciates the additional work done by the committee in reviewing the supplementary clinical studies provided and taking on board some of the feedback from clinicians and patients. However, we believe limiting the guidance to use of the treatment in the way described is not in the best interests of UK patients with dysphagia post stroke for the following reasons: 1. The severe dysphagia post stroke in patients with a tracheostomy tube (treated in the PHAST TRAC study for example) is not a different type of severe dysphagia post stroke that is present in patients without a tracheostomy. This is an entirely artificial distinction and one that is not made in real world clinical practice. Patients are assessed and managed based on the common symptoms of severe dysphagia seen through instrumental exam - compromised airway protection, poor secretion management and lack of effective swallowing activity. The PHAST TRAC study showed the additional benefit of early decannulation following the significant improvement in dysphagia symptoms. The Phagenyx treatment does not rely on the presence of a tracheostomy tube to achieve its therapeutic effect. Withholding the treatment from patients because they do not have a tracheostomy tube does not make sense in the	Thank you for your comments. The committee considered this comment but decided not to change the subgroup defined in the 'special arrangements' recommendation. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'. The committee considered subgroups as described in the evidence in the overview. Analyses presented outcomes for subgroups of people with and without tracheostomy. The section called 'Why the committee made these decisions' explains that the strongest evidence of efficacy is for decannulation, meaning that the person would need to have a tracheostomy for the procedure to show efficacy. The guidance acknowledges that the committee do not have concerns about the safety of the device in the 'Why the committee made these recommendations' section. The definition of 'special arrangements' in the Interventional Procedures Programme Manual states "The

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			context of real world care. The US FDA recently approved Phagenyx for treatment of all patients with severe dysphagia post stroke for exactly this reason. 2. The company understands and appreciates that NICE have a duty of care to be both accurate and clear in the guidance provided in order to protect patients, users and healthcare systems. With that in mind however, the Phagenyx System clearly does not meet the NICE definition of special arrangements. As written, this definition requires an uncertainty about ""safety AND effectiveness"" or evidence of ""risks of serious harm"". This is categorically not the case for the Phagenyx System and is both inaccurate and misleading for any interested party reviewing NICE guidance. The Phagenyx System has a safety record that includes over 10 years routine clinical use treating over 3000 patients, multiple clinical studies including RCTs gathering detailed adverse event data over 25 years without a single serious adverse event linked to Phagenyx treatment, and therefore is not consistent with this special arrangements statement. It's also not internally consistent with the NICE statement in section 1.7 of the draft guidance which states "There are no safety concerns about pharyngeal electrical stimulation". 3. The Phagenyx System is the only treatment that directly targets the neurological component of neurogenic dysphagia. There are no other treatment options to address this aspect of dysphagia. In the US, the FDA have designated Phagenyx as a Breakthrough Device - a new and innovative therapy that is the only evidence-based treatment option to address a substantial unmet clinical need. They have also agreed to re-imburse 65% of the cost the device for 3 years to try and drive usage and uptake in US healthcare systems. As a result of implied safety concerns in NICE guidance and a requirement as a result to include clinical governance and data collection, it is undoubtedly the case that UK sites will	Committee recommends these arrangements when using a procedure because there are significant uncertainties in the evidence on efficacy **or** safety, **or** an inadequate quantity of evidence". A 'research only' recommendation is made when 'the level of uncertainty about the efficacy **or** safety evidence is such that it is considered to be in the best interest of patients to recommend controlled investigation of the procedure under the scrutiny and protection of research ethics committees'.

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			not use this treatment. We have already been informed by existing sites that use Phagenyx that they plan to stop its use based on the draft NICE guidance alone. As a result of the draft NICE guidancea, a demonstrably safe treatment that represents the only available treatment option is going to be withheld from patients in the UK. The company believes that the committee do not fully appreciate the negative consequences that this guidance will have on the UK patient community.	
9	Consultee 5 Phagenesis Ltd	**1.2**	Given the CE/MDR certification of the devices, lack of safety concerns and inclusion in national and international guidelines, clinicians intending to use Phagenyx with their patients should not be required to seek additional clinical governance approvals. This guidance is very likely to pose additional barriers to clinicians wanting to adopt the treatment, and thus, potentially limit patients' access to a treatment when there is no alternative option for dysphagia rehabilitation, despite no safety concerns.	Thank you for your comment. The section of the guidance called 'Why the committee made these recommendations' explains that the special arrangements recommendation has been made because of uncertainty about the efficacy of the procedure. This recommendation encourages the additional research that is needed to reduce uncertainty about the efficacy of this procedure.
10	Consultee 5 Phagenesis Ltd	**1.3**	Creating a system for all users to submit data on all post stroke tracheotomised patients treated is a major burden for healthcare companies, hospitals and clinical professionals and is not warranted based on the safety record of the device and its use in routine clinical practice for over 10 years. Treatment of tracheotomised patients with dysphagia using Pharyngeal Electrical Stimulation for example is already a component part of Tracheostomy best practice guidelines in the UK and Germany. Requiring a mandatory post market registry to collect outcomes data in these patients is inconsistent with this status.	Thank you for your comment. The section of the guidance called 'Why the committee made these recommendations' explains that the special arrangements recommendation has been made because of uncertainty about the efficacy of the procedure. This recommendation encourages the additional research that is needed to reduce uncertainty about the efficacy of this procedure. When making their decision, the committee considered recommendations from other

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				guidelines, which were presented in the overview.
11	Consultee 6 NHS Professional	**1.1**	The PES has been shown to reduce the need for a PEG in a number of patients in our cohort without a tracheostomy. This has meant that patients who are dysphagic but are able to manage their own secretions have avoided needing nursing home/ district nursing care to manage the PEG in the community. It opens out the choice for potential to be discharged home and reduces the load on after hospital care; for this reason it is my comment that PES be indicated for a wider range of patients including those not requiring a tracheostomy.	Thank you for your comment. The committee considered this comment but decided not to change the subgroup defined in the 'special arrangements' recommendation. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.
Changes to the wording of 1.4				
12	Consultee 7 NHS Professional	1.4	Thorough assessment via videofluoroscopy could also be used. Robust assessment is required to ensure the nature and aetiology of the dysphagia is fully undersood. An instrumenal assessment of sorts is required, but this could be Videofluoroscopy or FEES (endoscopy).	Thank you for your comment. The following changes were made to section 1.4: "Patient selection should be done by healthcare professionals experienced in managing neurogenic dysphagia with specific training in the procedure. An endoscopic *or videofluoroscopic* assessment maybe used"**.**

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13	Consultee 2 NHS professional	1.4	e.g. Flexible Endoscopic Evaluation of swallowing, by a speech and language therapist.	Thank you for your comment. In line with comment 12, the following changes to section 1.4 were made: “Patient selection should be done by healthcare professionals experienced in managing neurogenic dysphagia with specific training in the procedure. An endoscopic *or videofluoroscopic* assessment may be used”. The information for use for the device used in this procedure does not specify what type of healthcare professional should do the procedure, therefore this has not been specified in the guidance.
Comments disagreeing with draft recommendations 1.6 and 1.7				
14	Consultee 2 NHS professional	1.6	These patients are being regularly treated in clinical practice with positive outcomes. I have personally treated 3 patients with acute brain stem and basal ganglia infarcts who have experienced remarkable recoveries in swallow safety post pharyngeal electrical stimulation. 2 gastrostomies were avoided, the other gastrostomy is no longer in use as a result of the treatment. All 3 returned to oral intake with no requirement for alternative feeding. none of these patient has a tracheostomy.	Thank you for your comment. The committee considered this comment but decided not to change the ‘research only’ recommendation. The rationale is detailed in the section of the guidance called ‘Why the committee made these recommendations’. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.

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15	Consultee 8 Parkinson's UK	**n/a**	We welcome the opportunity to comment on this guidance as there are limited treatment options for people with Parkinson's who experience neurogenic dysphagia and we believe this intervention could be life-changing for some people with the condition. However we recognise there is limited evidence on its effectiveness for people with other causes of neurogenic dysphagia as the draft recommendations note. While we understand the cautiousness around the recommendation in 1.6 only to offer this intervention in research, however we would urge NICE to consider whether it could be offered as a procedure for people using the special arrangements approach. Having it as research only with the need for a formal study might reduce the ability to gather intelligence on its effectiveness. This review of quality of dysphagia care for people with Parkinson's (https://www.ncepod.org.uk/2021dysphagia/Dysphagia%20in%20people%20with%20PD_Hard%20to%20Swallow_Full%20report.pdf) gives a fairly recent snapshot of the interventions and strategies Speech and Language Therapists (SaLTs) use to treat people with the condition. Many of the treatment options and interventions are well established but not routinely offered in the practice of the majority of SaLTs who treat people with the condition in the UK. For instance the UK Parkinson's Audit (2022, https://www.parkinsons.org.uk/sites/default/files/2023-	Thank you for your comments. The consultee agrees there is limited evidence for PES in people with Parkinson's who experience neurogenic dysphagia. The consultee agrees that more research is needed but states that the research only recommendation may restrict the ability to collect more data. The 'Why the committee made these recommendations' section of the draft guidance states that the research only recommendation was made because of uncertainty about the efficacy of PES in this group. Section 1.7 describes what further research is required to reduce this uncertainty. The committee acknowledged that treatment options are limited in the 'Why the committee made these recommendations' section of the guidance. The review by the National Confidential Enquiry into Patient Outcome and Death (2021) does not mention use of PES. The audit by Parkinson's UK (2022) is not a peer review publication and does not mention PES. The review by Lopez-Liria et al. (2020) describes neuromuscular electrical stimulation but all papers in reference to this were transcutaneous electrical stimulation, not PES, therefore out of the remit of this topic.

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			06/2022%20Audit%20-%20Complete%20Data%20Tables%20%20%281%29.pdf) shows that a small percentage of people with Parkinson's benefit from non-traditional interventions such as Expiratory Muscle Strength Training (ESMT). 1.9% of patients in the audit benefitted from ESMT, in comparison to the more traditional fluid and diet modification, which is used in 49.8% of cases, postural changes in 44.9% of patients and strategies for safer swallowing which is used in 62.1% of patients. There are limitations with this data as only 10 patients per service are audited, but it does give an indication of interventions that are currently used for people with Parkinson's. It is worth noting that ESMT has taken around 10 years to get into regular practice for SaLTs and it's clear from the Parkinson's Audit data that there needs to be greater training for professionals to enable them to offer it to their patients with Parkinson's. This review (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7312221/) summarises effective treatment options for people who experience dysphagia in Parkinson's and notes the importance of swallowing interventions that aid rehabilitation. The review also notes that neuromuscular electrical stimulation (NEMS) along with ESMT 'have been successful in swallowing and reducing the risk of choking, aspiration or improving oropharyngeal function'. However in the latter technology the evidence is limited. We believe there is an unmet need in the Parkinson's population for the use of PES and NEMS due to the age	The draft guidance states that specific training would be needed to implement this procedure, in section 1.5.

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			profile of the condition. While the majority of people living with Parkinson's are over 65, at least 9,000 people with the condition are under 50. This intervention could rehabilitate their swallow, and would enable people to live a more fulfilling life without the need to modify their food and drink intake for the rest of their life. However we recognise there needs to be more research to understand the dosage and protocol for individuals, especially due to how the condition affects everyone differently. Also we believe there would need to be a wide ranging programme of training on the intervention; and additional investment in the equipment to ensure consistent access to the technology across the country, especially in community settings."	
16	Consultee 7 NHS Professional	**1.6**	I think this really limits the numbers of patients who could benefit. The key factors needs to be a severe dysphagia of neurological origin that is not progressive. There isn't enough known yet about PES in progressive neurological conditions, but the treatment has benefitted many patients with dysphagia due to stroke, brain injury, post critical care/intubations at times when nothing else has. Many of these people will have had tracheostomies, but may have already been decannulated or others wouldn't have needed tracheostomy. Recommendations for PES for use with people post stroke + tracheostomy are great, but too limited in my opinion. We've seen many great outcomes in patients who have had long critical care stays and long periods of intubation +/- tracheostomy, but who have not had a stroke. There is also evidence supporting this. The current recommendations would deny them this treatment and have a significant impact on quality of life and future care needs. Conversely, many patients post stroke or brain injury without tracheostomy are now able to eat and drink as a result of PES alone.	Thank you for your comments. The committee considered this comment but decided not to change the recommendations. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.

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17	Consultee 4 NHS Professional	1.6	WHY??? we currently have very little therapeutically to offer patients who have a sensory deficit within their dysphagia profile. This is making a possible treatment unavailable to many unless specifically involved in clinical trials. In our trial of this treatment (currently 9 patients) we have treated 1 patient who is 12 months post-stroke, who has been NBM since CVA with a PEG, and had 6 admissions to hospital with aspiration pneumonia from his secretions. Since having PES he progressed within 4 weeks to full oral intake of normal diet and fluids and in the 3 months since treatment has completed has had no chest infections, and is due to have his PEG removed in a few weeks time. We have also treated acute stroke patients who do not have a tracheostomy for whom therapy focusing on motor deficits was not improving the sensory deficit and therefore they were still aspirating as not aware of secretions or food/fluid material entering their larynx prior to swallow being triggered. This treatment is essential as a tool to either stand alone for someone with a purely sensory pharyngeal dysphagia, or as a combined treatment with other more traditional swallow therapies focusing on motor components of swallowing difficulties. We have also given this treatment to a head injury patient and a patient who suffered neurogenic dysphagia following surgery for a brain tumour, who both presented with sensory and motor dysphagias	Thank you for your comment. The committee considered this comment but decided not to change the recommendations. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'. The committee acknowledged that treatment options are limited in the 'Why the committee made these recommendations' section of the guidance. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.
18	Consultee 4 NHS Professional	1.7	Why only research? The parameters of 1.7 regarding this treatment are core to any patient selection and ensuring patient safety during treatment, as we would do with any clinical procedure or treatment we use with patients, such as a FEES (fiberoptic endoscopic evaluation of swallow). The cost of the catheter means patient selection is key not only to ensure patient safety, but to ensure best use of resources, and to balance patient and family expectations for the treatment - it is excellent for some but clearly not clinically indicated for a number of dysphagic patients. In our own	Thank you for your comments. The 'Why the committee made these recommendations' section of the draft guidance explains that the evidence of efficacy is not clear in people with neurogenic dysphagia after stroke who do not have a tracheostomy, and that there is not enough evidence of efficacy for people with other causes of neurogenic

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			experience we have also had to manage the expectations of our consultant colleagues who thought this would be a 'game changer' for all dysphagic patients, which it is not, but it definitely is for some.	dysphagia, to know what elements of patient selection make this procedure efficacious. The draft recommendations in 1.6 and 1.7 ask for more research to demonstrate this.
19	Consultee 5 Phagenesis Ltd	**1.6**	The company agrees in part with this determination based on clinical evidence and clinical practice: 1. As highlighted in the company response to section 1.1, separating patients that have severe dysphagia post stroke and still remain tracheotomised and those with severe dysphagia post stroke that do not have or no longer have a tracheostomy tube in place is an entirely artificial distinction. The general sequence of events post stroke is that patients that require mechanical ventilation are orally intubated and then over time either extubated following weaning (at which point they may be seen to have dysphagia) or tracheotomised for an additional period before weaning (at which point they may be seen to have dysphagia) or decannulation (at which point they may be seen to have dysphagia). The neurogenic dysphagia they present with will be a combination of deficits dues to the original stroke which may be further exacerbated by the prolonged presence of oral and/or tracheotomy tubes. For this reason patients with dysphagia post stroke that have also been ventilated and tracheotomised thereafter are the most complex and difficult to treat (central deficits additionally complicated by peripheral desensitisation and/or mechanical demage due to the breathing tube). Dysphagia assessment via instrumental exam however follows a standard process for all of these patients and treatment options chosen based on common symptoms of dysphagia. These patients are not segmented clinically based on actual or historical ventilation tube status - they are treated based upon their dysphagia. If a patient has a severe stroke with dysphagia but did not require mechanical ventilation they are not assessed differently and they are not managed differently.	Thank you for your comments. The committee considered subgroups as described in the evidence in the overview. Analyses presented outcomes for subgroups of people with and without tracheostomy. In the 'Why the committee made these decisions' explains that the strongest evidence of efficacy is for decannulation, meaning that the person would need to have a tracheostomy for the procedure to show efficacy. The company agrees that there is less evidence of efficacy for people with other causes of neurogenic dysphagia. The company state they are committed to further data collection in these groups.

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			2. The company agrees that there is less evidence for the benefit of Phagenyx treatment in patients with neurogenic dysphagia arising as a consequence of conditions or events other than stroke including traumatic brain injury and progressive neurological diseases (although the PHADER Study provided safety data for these other groups). The company is committed to gathering further data through a post market registry to build a clearer picture of treatment benefits. This is currently under design.	
20	Consultee 5 Phagenesis Ltd	**1.7**	The treatment protocol has been established with this device, and is 10 minutes per day x 3 sessions, with the potential to offer a further 3 sessions (10 minutes per session) if required. This was established through functional brain imaging studies dose response studies and controlled clinical studies over 20 years ago and with respect does not constitute an open research question. As highlighted previously the company agrees with the committee if that group 1 is defined as 'patients with severe dysphagia post stroke' but not if limited to those that are additionally tracheotomised at the point of treatment for the reasons highlighted in sections 1.1 and 1.6. The clinical trial and registry data showed that the symptoms of dysphagia could be improved significantly and sufficiently such that the additional benefit of early safe tracheostomy tube decannulation could be carried out. The measures used to make the decannulation decision were all related however to the dysphagia status of the patient and were a comprehensive assessment of swallowing safety. The company respectfully disagrees with the committee statement that additional clinical efficacy outcomes are needed to demonstrate significant improvements in swallow	Thank you for your comments. The company states that the treatment protocol is established. The following change has been made to the wording of the treatment protocol in 2.3 in line with other comments submitted by company and consultees: “Treatment is given by a healthcare professional with appropriate training and typically *a treatment cycle* consists of 10 minutes of stimulation each day for ~~6~~ *3* consecutive days*, for up to 2 cycles*.” The committee considered subgroups as described in the evidence in the overview. Analyses presented outcomes for subgroups of people with and without tracheostomy. In the ‘Why the committee made these decisions’ explains that the strongest evidence of efficacy is for decannulation, meaning that the person would need to have a tracheostomy for the procedure to show efficacy.

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			safety following treatment. As stated previously, the company does not agree that an artifical distinction can or should be made between patients with severe dysphagia post stroke that have a tracheotomy tube in place at the point of treatment and patients with severe dysphagia post stroke that do not have a tracheostomy tube in place at the point of treatment. The efficacy of the treatment in improving the dysphagia symptoms to the point of restoring a safe airway is not reliant on the presence of a tracheotomy tube. As written the guidance would allow the use of the treatment in a tracheotomised patient with dysphagia post stroke but prevent its use in the same patient with the same dysphagia once the tube was removed.	The committee considered both decannulation and swallow safety outcomes in the evidence, as presented in the overview.
Other comments disagreeing with draft recommendations made in section 1				
21	Consultee 9 NHS Professional and Phagenesis co-founder	**1**	Draft recommendation: I believe IPAC have drafted a far too restrictive and conservative recommendation for this technology. Given that IPAC have clearly indicated in the sections below that the technology is safe, it seem strange that they still argue for special arrangements for stroke and trachecotomy related dysphagia and research for all other forms of neurogenic dysphagia. Rather, I would have expected that IPAC would follow RCP stroke guidelines and recommend unrestricted use of pharyngeal electrical stimulation for tracheotomy and stroke associated dysphagia, where the evidence is fairly strong (RCT level) and comparably better that other technologies in this field. I would contend that non-progressive forms of neurogenic dysphagia (stroke, TBI, critical illness polyneuropathy) be given special arrangements - here the data are good with convincing real world evidence, supported by meta-analyses, and observational studies. I would suggest that progressive forms of neurogenic dysphagia (Parkinson's, ALS etc) fall under research only. Such a more considered	Thank you for your comment. The committee considered this comment but decided not to change the recommendations. The rationale is detailed in the section of the guidance called 'Why the committee made these recommendations'. The guidance acknowledges that the committee do not have concerns about the safety of the device in the 'Why the committee made these recommendations' section. The definition of special arrangements in the Interventional Procedures Programme Manual states "The Committee recommends these arrangements when using a procedure because there are significant uncertainties in the evidence on efficacy **or** safety, **or** an inadequate quantity of

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			recommendation as stated above would allow clinicians to use this technology in a more realistic way within the NHS, in patients who have little or no alternative (I note the comments from patients who have had this treatment which is overwhelmingly positive), rather that place undue and unnecessary difficulties and regulatory restrictions on what is a CE marked/FDA approved and relatively well studied technology. IPAC should consider both the clinical impact of their current recommendation draft and the untended negative effects of such a recommendation on clinical practice.	evidence". The 'Why the committee made these recommendations' section of the guidance explains that the special arrangements recommendation has been made because more evidence about the efficacy of the procedure is needed. This recommendation encourages the additional research that is needed to demonstrate the efficacy of this procedure. The 'Why the committee made these recommendations' section of the guidance explains that the research only recommendation was made because there was uncertainty and a lack of evidence in other outcomes. When making their decision, the committee considered recommendations from other guidelines, which were presented in the overview.
Comments on the description of neurogenic dysphagia and PES				
22	Consultee 9 NHS Professional and Phagenesis co-founder	**Description**	Description: This appears a reasonable summary.	Thank you for your comment.
23	Consultee 2 NHS Professional	**Description**	Not only do patients with severe dysphagia require a tracheostomy due to saliva management difficulties, some patients experience neurogenic dysphagia as a direct result of prolonged endotracheal tube placement or tracheostomy tube placement when the cuff is inflated.	Thank you for your comment. The consultee suggests amending the description to reflect that neurogenic dysphagia can be caused by prolonged endotracheal tube placement or tracheostomy tube placement with inflated cuff. In line with other similar comments, the following changes have been made to the description: "Neurogenic dysphagia

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				is difficulty swallowing (dysphagia) caused by conditions that affect the nervous system (neurogenic), for example, stroke, multiple sclerosis and Parkinson's disease. *It can also be caused by major head and neck surgery (for example, to remove cancer), trauma, and intensive care treatment (intubation and tracheostomy).* *Dysphagia* ~~It~~ can cause coughing and choking, and food or drink may go into the lungs, which can lead to chest infections. People with severe dysphagia may need a tracheostomy *to help prevent saliva going into the lungs*." Please note that this wording is removed from the main guidance for publication but used for the Information for the Public.
24	Consultee 2 NHS Professional	**Description**	Improve swallow safety, secretion management and quality of life.	Thank you for your comment. The consultee suggests changes to the procedure description. In line with this and comment 28, the following wording has been changed: "The aim is to improve swallowing ~~and reduce other symptoms~~ *, reduce aspiration and improve secretion management and quality of life*." Please note that this wording is removed from the main guidance for publication but used for the Information for the Public.
25	Consultee 2 NHS Professional	**Description**	These are neurodegenerative conditions and should not be categorised in the same way as stroke.	Thank you for your comment. The remit of this topic is neurogenic dysphagia which includes dysphagia caused by the conditions listed within the description. Experts

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				and stakeholders were consulted when deciding the scope of the guidance.
26	Consultee 2 NHS Professional	**Why the committee made these recommendations**	e.g. post prolonged ETT and tracheostomy placement - these patient's cause of intubation and ventilation may having nothing to do with a swallowing difficulty. The dysphagia occurs as a direct result of their life saving treatment.	Thank you for your comment. The consultee notes that neurogenic dysphagia can be caused by prolonged intubation and tracheostomy placement. This detail has been added to the description of neurogenic dysphagia in response to comment 23.
27	Consultee 5 Phagenesis Ltd	**2.1**	This is not technically correct. Neurogenic dysphagia is caused by damage to, or disruption of the neurological systems for control and coordination of swallowing, not muscles. Causes can include stroke, TBI, progressive diseases, development disorders and desensitisation of the peripheral swallow sensorium following mechanical ventilation. Other types of non-neurological dysphagia can be caused by mechanical trauma, surgery, cancer or muscle atrophy due to prolonged disuse	Thank you for your comment. The consultee states that neurogenic dysphagia is caused by damage or disruption of the nerves not the muscles. In line with this and similar changes to the description the following changes have been made to 2.1: 'Difficulty in swallowing (dysphagia) is ~~can be~~ caused by neurological impairment ~~muscles of the pharynx~~. It can happen because of several conditions, including stroke, traumatic brain injury, disorders of cerebral development, neurodegenerative diseases, major head and neck surgery (for example, to remove cancer), and intensive care treatment (intubation and tracheostomy).'
28	Consultee 5 Phagenesis Ltd	**Description**	The current description of neurogenic dysphagia is limiting as it only highlights neurogenic dysphagia caused by examples of central deficits. A holistic description would include neurogenic dysphagia as a result of peripheral damage too, for example, prolonged intubation causing de-sensitisation. An alternative, more inclusive wording has been proposed here: Neurogenic dysphagia is difficulty	Thank you for your comments. The company states that the description of neurogenic dysphagia does not capture all causes. In line with this and other similar comments, the following changes have been

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			swallowing (dysphagia) caused by conditions that affect the nervous system (neurogenic), for example, stroke, multiple sclerosis and Parkinson's disease. It can also arise over time due to the presence of a breathing tube in the throat because the nerves there become de-sensitised. Dysphagia can cause coughing and choking, and food or drink may go into the lungs, which can lead to chest infections. As a result, patients frequently have to fed via a tube and cannot eat and drink normally until the dysphagia gets better. The description of Pharyngeal Electrical Stimulation (PES) is also overly reductionist and as such, a more comprehensive yet lay explanation has been proposed: NICE is looking at pharyngeal electrical stimulation for neurogenic dysphagia. In this procedure a catheter is passed through the nose and into the throat. The catheter delivers small amounts of electrical current to the pharynx. This stimulation is optimised for each patient to overcome any desensitisation in the throat and to travel to the parts of the brain involved in swallowing control where it stimulates those areas also. The aim of treatment is to restore the control, effectiveness and safety of swallowing."	made to the description: "Neurogenic dysphagia is difficulty swallowing (dysphagia) caused by conditions that affect the nervous system (neurogenic), for example, stroke, multiple sclerosis and Parkinson's disease. *It can also be caused by major head and neck surgery (for example, to remove cancer), trauma, and intensive care treatment (intubation and tracheostomy). Dysphagia* ~~It~~ can cause coughing and choking, and food or drink may go into the lungs, which can lead to chest infections. People with severe dysphagia may need a tracheostomy *to help prevent saliva going into the lungs*." Please note that this wording is removed from the main guidance for publication but used for the Information for the Public. The company states that the description of the procedure misses information about how it is performed and the aim. In line with this and other similar comments, the following changes have been made to the wording: "The aim is to improve swallowing ~~and other symptoms ,~~ *reduce aspiration and improve secretion management and quality of life*." Please note that this wording is removed from the main guidance for publication but used for the Information for the Public.
29	Consultee 5 Phagenesis Ltd	**2.2**	Existing dysphagia care broadly segments into two categories - compensatory management and rehabilitation. Compensatory strategies attempt to deal with the symptoms of dysphagia, but do not act therapeutically - tube feeding and positioning during feeding fall into this category; they are not treatments. Rehabilitation strategies such as swallowing	Thank you for your comment. The following changes have been made to the description of current treatment in section 2.2 of the guidance and the overview, to reflect the difference between compensatory and

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			exercises, require substantial patient involvement and compliance to achieve their effects. Transcutaneous neuromuscular electrical stimulation (NMES) can be effective in some cases where prolonged swallowing has led to muscle atrophy due to disuse, but it does not directly act on neurological systems for swallowing. There are currently no treatment options other than Phagenyx (PES) that directly target the neurological component of neurogenic dysphagia.	rehabilitation strategies and to mention transcutaneous neuromuscular treatment options: “Treatment options depend on the cause and severity of the dysphagia. *Compensatory strategies* ~~treatments~~ include diet modification (including thicker fluids and foods) *and in moderate or severe cases, nasogastric tubes, percutaneous endoscopic gastrostomy tubes or jejunostomy tubes may be used to provide nutritional support. Rehabilitation strategies include* swallowing therapy (to help relearn swallowing and strengthen muscles) *and in some cases*, t*ranscutaneous neuromuscular stimulation.* ~~In severe cases, nasogastric tubes or percutaneous endoscopic gastrostomy tubes may be used to provide nutritional support.~~ “. Please note that this wording is removed from the main guidance for publication but used for the Information for the Public and reflected in the overview.
30	Consultee 5 Phagenesis Ltd	**2.3**	The standard treatment protocol is 10 mins per day for up to 6 days	Thank you for your comment. The consultee states the treatment protocol is 10 mins per day for up to 6 days. The following change has been made to the wording of the treatment protocol in 2.3 in line with other comments submitted by company and consultees: “Treatment is given by a healthcare professional with appropriate training and typically *a treatment cycle* consists of 10 minutes of stimulation each day for ~~6~~ *3* consecutive days*, for up to 2 cycles*.”

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31	Consultee 9 NHS Professional and Phagenesis co-founder	**2.3**	2.3: The treatment schedule should say "for 3 or 6 consecutive days".	Thank you for your comment. The following change has been made to the wording of the treatment protocol in 2.3 in line with other comments submitted by company and consultees: “Treatment is given by a healthcare professional with appropriate training and typically *a treatment cycle* consists of 10 minutes of stimulation each day for ~~6~~ *3* consecutive days*, for up to 2 cycles*.”
Other comments on the draft recommendations				
32	Consultee 4 NHS Professional	**Unmet need**	As speech therapists we have very little we can offer to patients who have a sensory dysphagia so all therapy is focused on motor elements of the disorder with the hope sensation will improve with motor function - this treatment has improved pharyngeal sensation of secretions and food/fluid residue in all the 9 patients we have currently trialed it with including 2 who had had dysphagia for a year, and have suffered all these elements as an outcome of having a significant dysphagia	Thank you for your comment. The committee acknowledged that treatment options are limited in the ’Why the committee made these recommendations’ section of the guidance. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.
33	Consultee 5 Phagenesis Ltd	**3.2**	The studies that involved patients with post stroke dysphagia were assessed on their swallowing safety using the Warnecke algorithm - secretions with or without aspiration,	Thank you for your comment.

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			spontaneous swallows and effective clearance. The decannulation event was secondary to this. The lack of reintubations was a measure of the persistence of treatment effect (i.e., the improvement in swallow function and safety did not diminish over time)	The committee considered evidence in the overview that reported both swallowing and decannulation outcomes.
34	Consultee 4 NHS Professional	3.3	Patients being considered for this treatment are likely to already have had an NGT in situ due to dysphagia so the risks of discomfort and injury are similar to those associated with NGT placement, which should be risk assessed before being placed. The stimulation catheter is recommended to have a bridle used with it, to help reduce risk of displacement as it is heavier than an NGT alone, but again the risks of nasal bridle use should always also be assessed, and will be exactly the same as if a bridle is needed for an NGT alone. In regards to aspiration, the placement of the catheter is unlikely to increase aspiration, as again patients likely to already have an NGT in situ. Increased sensation to pooled secretions following this treatment is much more likely to reduce the risk of aspiration than increase it.	Thank you for your comment. The committee acknowledges the safety profile of the procedure in the 'Why the committee made these recommendations' section. Section 3.2 and 3.3 are to explain what outcomes were considered when assessing the evidence of efficacy and safety, respectively.
35	Consultee 4 NHS Professional	3.4	Could you please discuss this treatment with our 'old' stroke patient - it has changed his long term outcome as was NBM with PEG insitu having failed to progress with traditional voice therapy over the previous 11 months post CVA. NICE needs to put out a new call for patients to comment following this treatment/experiences - 9 patients is not enough feedback from across the hospitals now trialing this treatment - I am happy to send you our summary sheets or more in-depth information as needed on request. I feel very strongly to limit this to such a small group of patients when we have had such good direct experience is potentially preventing patients recovering their swallow and being a drain on NHS resources for a much longer period, in addition to the social and personal changes this will cause the patients and their families.	Thank you for your comment. The committee can only consider published evidence in their assessment of clinical efficacy. Patient commentary and professional expert opinion is used to guide the committee in understanding the context of the research findings. Section 3.4 of the guidance states that NICE received 9 patient commentaries that were considered alongside the evidence in the overview. One additional patient submission was received and considered by the committee. This has been noted in section 3.4.

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36	Consultee 5 Phagenesis Ltd	**3.6**	Correction: There is no other Registry ongoing at present. PhINEST is ongoing and is an RCT assessing the benefits of PES (Phagenyx) on post-extubation dysphagia in mixed ICU patients.	Thank you for your comment. The company report that PhINEST is an ongoing RCT. The ongoing research reported in 3.6 of the draft guidance will be clarified to read: 'There is a large ongoing RCT being done in people with stroke without a tracheostomy. This is due to complete in 2025 (PHEAST study). There is an ongoing RCT in people with post-extubation dysphagia that is due to complete in 2025 (PhINEST study).'
Comments on the overview				
37	Consultee 5 Phagenesis Ltd	**Page 3 to 4 of the overview (Indications and current treatment)**	As per 2.2, Existing dysphagia care broadly segments into two categories - compensatory management and rehabilitation. Compensatory strategies attempt to deal with the symptoms of dysphagia but do not act therapeutically - tube feeding and positioning during feeding fall into this category; they are not treatments. Rehabilitation strategies such as swallowing exercises require substantial patient involvement and compliance to achieve their effects. Transcutaneous neuromuscular electrical stimulation (NMES) can be effective in some cases where prolonged swallowing has led to muscle atrophy due to disuse, but it does not directly act on neurological systems for swallowing. There are currently no treatment options other than Phagenyx (PES) that directly target the neurological component of neurogenic dysphagia.	Thank you for your comment. The following changes have been made to the description of current treatment, to reflect the difference between compensatory and rehabilitation strategies and to mention transcutaneous neuromuscular treatment options: "Treatment options depend on the cause and severity of the dysphagia. *Compensatory strategies* include diet modification (including thicker fluids and foods) *and in moderate or severe cases, nasogastric tubes, percutaneous endoscopic gastrostomy tubes or jejunostomy tubes may be used to provide nutritional support. Rehabilitation strategies include* swallowing therapy (to help relearn swallowing and strengthen muscles) *and in some cases, transcutaneous neuromuscular stimulation* ~~in severe cases, nasogastric tubes or percutaneous endoscopic~~

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				~~gastrostomy tubes may be used to provide nutritional support.~~
38	Consultee 5 Phagenesis Ltd	**Page 4 of the overview (What the procedure involves)**	CORRECTION: the treatment can be provided for up to 2 cycles of treatment (up to 6 days x 10 minutes)	Thank you for your comment. The following change has been made to the wording of the treatment protocol in 2.3 in line with other comments submitted by company and consultees: “Treatment is given by a healthcare professional with appropriate training and typically *a treatment cycle* consists of 10 minutes of stimulation each day for ~~6~~ *3* consecutive days*, for up to 2 cycles*.”
39	Consultee 5 Phagenesis Ltd	**Page 6 of the overview (Outcome measures- MCID)**	This has been included following previous comments but this is not an endpoint. It is not specific to DSRS or our treatment and thus isn't relevant to be included in this section	Thank you for your comment. MCID was included in the outcome measures section of the overview to help readers to understand outcomes from the Bath (2020) study that refer to MCID.
40	Consultee 5 Phagenesis Ltd	**Page 8 of the overview (Efficacy summary- Decannulation)**	"PHADER: Majority of the n=66 decannulated patients had Stroke, but this is the split of stroke vs. non-Stroke patients. Stroke n=38 Ventilator-associated n=18 TBI n=10 This is important to note in relation to your comments regarding who did and did not have a stroke in the PHADER study. Please also note that there were no recannulations in the PHAST-TRAC or Suntrup studies."	Thank you for your comment. The company have provided additional information on the cause of dysphagia in the group of people included in the decannulation outcome of the PHADER study (Bath, 2020). This information has been added to the overview and the committee considered this information when making their decision.
41	Consultee 5 Phagenesis Ltd	**Page 11 of the overview (Efficacy**	Leaking and residues as a measure does not acknowledge or include comments relating to secretion severity and pooling. Inclusion of secretion severity and pooling may	Thank you for your comment.

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		summary- Leaking and residues)	expand this section to further understand the benefits of this treatment.	The company report that the leaking and residues outcome reported in Hermann (2022) does not include information about secretion severity and pooling. The overview reports all outcomes that were reported in this study. Other swallowing outcomes are reported in the efficacy section of the overview.
42	Consultee 5 Phagenesis Ltd	**Page 13 of the overview (Overall rate of adverse events).**	In the RCT of 162 people (87 on active treatment) with post-stroke dysphagia, there was no statistically significant difference in the rate of serious adverse events (SAEs) at the end of follow up. This further supports the safety status of the treatment and brings to question the inconsistencies relating to proposed guidance and the classification of special arrangements as 'questions around safety AND efficacy'.	Thank you for your comment. The company disagrees with the recommendations in section 1 of the guidance and refer to the RCT evidence by Bath (2016). This RCT was included in the evidence considered by the committee. The committee acknowledge that there are no safety concerns in the 'Why the committee made these recommendations' section of the guidance. The definition of special arrangements in the Interventional Procedures Programme Manual states "The Committee recommends these arrangements when using a procedure because there are significant uncertainties in the evidence on efficacy **or** safety, **or** an inadequate quantity of evidence".
43	Consultee 5 Phagenesis Ltd	**Page 13 of the overview (Device and treatment-unrelated adverse events)**	For information to further guide this comment relating to an SAE: PHADER: This patient had a prior history of difficult nasogastric tube insertions, producing copious secretions and coughing during such procedures that could have led to aspiration. In addition, the patient had also been experiencing recurring diarrhoea for two months and faecal impaction on abdominal x-rays that seemed to clear on repeat x-ray. Following detailed review of the event through the above-described standard adjudication process, this SAE	Thank you for your comment. This section of the overview reports "In the analysis of a prospective registry of 252 people with dysphagia from various neurological causes, there was 1 SAE (0.4%) that was considered possibly related to PES: pneumonia related to catheter insertion leading to sepsis (Bath 2020)". This reflects the wording of the publication and as the company describe, the

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			was conservatively adjudicated as having a “possible” relationship to the catheter insertion only, but was not deemed to have a causal relationship to PES-treatment or the Phagenyx devices.	classification of possible relationship to the treatment.
44	Consultee 5 Phagenesis Ltd	**Page 14 of the overview (Death)**	It must be noted here that none of the deaths were associated or related to device or PES, and were a reflection of the severity of the patients' illness	Thank you for your comment. This section of the overview reports that “None of the deaths were judged to be PES treatment or investigational device (base station and catheter) related (Dziewas 2018).”
45	Consultee 5 Phagenesis Ltd	**Page 14 of the overview (Anecdotal and theoretical adverse events)**	CORRECTION - we have no reports of eye pain in all of our report data. Please can you clarify this?	Thank you for your comment. The list of anecdotal and hypothetical adverse events in the overview is populated by feedback from professional expert questionnaires. NICE reports all theoretical and anecdotal adverse events that professional experts report on the questionnaire, that have not been covered by the literature reported in the main evidence.
46	Consultee 5 Phagenesis Ltd	**Page 9 of the overview (on PAS findings)**	As commented on previously, this study had many methodological problems that when corrected for in future studies (PHAST-TRAC, PHADER) resulted in positive patient outcomes.	Thank you for your comment. The committee considered the methodological limitations of the Bath (2016) study alongside the outcomes reported in the PHAST-TRAC and PHADER studies when making their decision.
47	Consultee 5 Phagenesis Ltd	**Page 45 of the overview**	Please note that the findings in the Bath trial (2016) were neutral, not 'negative' as described here	Thank you for your comment. The following text has been updated in the overview description of the Bath (2016) study: “The undertreatment of patients in the Bath

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				(2016) RCT may have contributed to the findings of this trial."
48	Consultee 5 Phagenesis Ltd	**Page 48 of the overview**	Please note, the PhINEST completion date is incorrect and should be changed to 'estimated December 2025'.	Thank you for your comment. The following text has been updated in the overview: "Expected recruitment is 360 people, estimated study end date is December 2025"

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."