Consultation comments on the draft scope and provisional stakeholder list for the assessment of PlGF-based testing to help diagnose suspected pre-eclampsia (Update of DG23) (provisional title)

Who	Section	Comment	NICE Response
Health professional	**Introduction/product properties** • Are these sections accurate and complete?	I think so	Thank you for your comment which we have considered.
Health professional	**Technologies** • Are the descriptions of the technologies accurate?	Need to be checked by the companies. Thresholds for the tests seem correct but no threshold listed for BRAHMS which mean it is not useable – not realistic for units to decide their own thresholds.	Thank you for your comment which we have considered.
Health professional	• Can any of the tests be used in a near patient setting (at point of care) in the NHS, or would they need to be done in a laboratory?	Quidel can be one using a point of care meter but is not a bedside test as centrifugation required.	Thank you for your comment which we have considered.
Health professional	• Are each of the technologies in use in the NHS and relevant to the evaluation?	Quidel and Roche currently in use. PerkinElmer in use for first trimester screening – I am uncertain if in use for diagnosis.	Thank you for your comment which we have considered.
Health professional	• Are there any other technologies with a similar purpose in use in the NHS?	Not that I am aware of.	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Health professional	**Target condition** • How should *suspected* pre-eclampsia be defined?	Women presenting with symptoms or signs which could be attributable to pre-eclampsia • New hypertension (>20 weeks gestation) or worsening chronic hypertension (requiring a change or commencement of antihypertensive therapy) • New proteinuria (>20 weeks) ≥30mg mmol/L on spot urine protein creatinine ratio or ≥ ++ on dipstick testing • Symptoms including frontal headache, visual disturbance, epigastric pain/pain under ribs, new nausea/vomiting (>20 weeks), new (rapid onset) hand/facial oedema • Abnormal biochemical or haematological parameters – elevated liver enzymes, elevated creatinine, low platelets • Additional features which might indicate pre-eclampsia/placental disease when present with any of the above – evidence of reduced fetal growth/size, oligohydramnios, abnormal uterine or umbilical Dopplers, shortness of breath	Thank you for your comment which we have considered. Section 3.1, (page 8) of the final scope has been amended to incorporate the information provided in this comment.

Who	Section	Comment	NICE Response
	• What distinguishes a person with suspected pre-eclampsia and someone with a diagnosis of the condition?	• The diagnosis of pre-eclampsia is made when one of the features above occurs in the presence of (new) hypertension – most commonly hypertension with proteinuria and/or abnormal blood tests and/or symptoms and/or concerns regarding fetal wellbeing on ultrasound scan. • The certainty of a diagnosis made on clinical features increases with the number of abnormal parameters present. • However, the clinical diagnosis is often not clear and the arbitrary thresholds will 'miss' many cases of true disease. For example, a small number of women will develop signs/symptoms of pre-eclampsia with sub diagnostic (ie <140/90mmHg) levels of blood pressure. • The clinical diagnosis is subjective and dynamic, especially in women with underlying medical disease (e.g. hypertension, renal disease, diabetes, autoimmune disease)	Thank you for your comment which we have considered. We have incorporated the information provided into section 3.1, page 9 of the final scope: 'A clinical expert commented that the diagnosis is subjective and dynamic, especially in women with underlying medical disease (such as hypertension, renal disease, diabetes or autoimmune disease). The clinical diagnosis of pre-eclampsia is often not clear and the thresholds used for clinical features such as blood pressure to indicate pre-eclampsia will miss many cases of true disease. For example, a small number of women will develop signs or symptoms of pre-eclampsia without hypertension(that is, with blood pressure less than140/90mmHg)'.
Health professional	**Care pathway** • If a person has a positive PlGF-based test result for pre-eclampsia, what changes to their care would occur?	Increased surveillance – usually 2-3 times per week as an outpatient or inpatient admission.	Thank you for your comment which we have considered.
Health professional	• Under what circumstances would someone have a repeat PlGF-based test if an initial test had been done and was negative?	No evidence to support repeat testing. Often repeated in clinical practice if the initial result was negative and there is a change in clinical condition triggering a new suspicion of pre-eclampsia.	Thank you for your comment which we have considered.
Health professional	**Population** • Is the population defined appropriately?	Yes	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Health professional	• Should people with severe hypertension (BP of 160/110 mmHg or more) be excluded from the population for this assessment (because they would be admitted to hospital regardless of their PlGF-based test result)?	No – blood pressure is dynamic. It depends how many readings above the threshold.	Thank you for your comment which we have considered. Women with severe hypertension (BP of 160/110 mmHg or more) remain included in the population for this assessment.
Health professional	• Are there groups within this population that should be considered separately?	The ones listed.	Thank you for your comment which we have considered.
Health professional	**Comparator** • Is this the most appropriate comparator for the assessment?	Yes	Thank you for your comment which we have considered.
Health professional	**Outcomes and costs** • Will these outcome and cost measures capture the most important benefits (and harms) of the technology?	Yes	Thank you for your comment which we have considered.
Health professional	**Equality** • NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed scope may need changing in order to meet these aims. In particular, please tell us if the proposed scope:		

Who	Section	Comment	NICE Response
Health professional	**Provisional stakeholder list** • Are there any stakeholders who should be invited to participate in the assessment?	No	Thank you for your comment which we have considered.
Health professional	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.	With regards to the hospital admission data there were actually 31,140 admissions for hypertensive disease in the data. Difficult to know how to interpret as uncertain how coded if occurred the hypertension was the same admission as the admission when birth occurred and 2/3 of cases occur after 37 weeks – need to consider carefully in any of this data were to be included in economic analyses. Also, as a caution regarding the quality of coding, several 'obstetric' admissions were in men (17000) and 27000 in children.	Thank you for your comment which we have considered. We have changed the wording in section 3.1, page 6 of the final scope to the following: 'According to the NHS digital's Hospital Admitted Patient Care Activity 2019-20 data, there were 10,547 admissions to hospital for pre-eclampsia and 211 for eclampsia between April 2019 and April 2020. However, a clinical expert cautioned that there may be some uncertainty in these data as they may not have captured everyone admitted with pre-eclampsia. Some women may have been classed as hypertensive disease admissions and so the actual number of pre-eclampsia admissions may be higher'.
Perkin Elmer	**Introduction/product properties** • Are these sections accurate and complete?	Yes	Thank you for your comment which we have considered.

Perkin Elmer	**Technologies** • Are the descriptions of the technologies accurate?	No. Please find below the corrections that are required: Page 1: "The PlGF tests measure the amount of placental growth factor (PlGF) in blood plasma **or serum.**" Page 2: "In normal pregnancy, PlGF levels rise and peak at 26 to 30 weeks gestation so the failure of PlGF levels to rise during pregnancy may be an indicator of placental dysfunction. In addition, some PlGF-based tests also measure soluble FMS-like tyrosine kinase-1 (sFlt-1), a protein which is thought to disable proteins, such as PlGF, which are associated with blood vessel formation. In people who develop pre-eclampsia, the levels of sFlt-1 are thought to be higher than those seen in normal pregnancy**. In normal pregnancy the level of sFlt-1 starts to rise after 28–32 weeks of gestation.** The tests are intended for use in conjunction with clinical judgement and other existing diagnostic tests, **to short-term prediction and to** aid the diagnosis of pre-eclampsia." Page 4: 2.2.3 DELFIA Xpress PlGF 1-2-3 test / DELFIA Xpress sFlt-1 kit (PerkinElmer) The DELFIA Xpress PlGF 1-2-3 can be used stand-alone test or together with DELFIA Xpress sFlt-1 test.	Thank you for your comments which we have considered. We have changed this sentence accordingly. See section 2.1, page 1 of the final scope. This section describes the purpose of the medical technologies as assessed within the scope of this work; that is, PlGF-based testing to help diagnose suspected pre-eclampsia. The full intended use of the DELFIA Xpress PlGF 1-2-3 test / DELFIA Xpress sFlt-1 kit is described in the scope in section 2.2.3, including that the ratio of sFlt-1/PlGF may be used as an aid in diagnosis of pre-eclampsia and for short term prediction of suspected pre-eclampsia together with other biochemical and clinical information. Section 2.2.3, page 4 of the final scope has been amended to reflect this.

		This kit is intended for the quantitative determination of Placental Growth Factor (PlGF) in maternal serum using the 6000 DELFIA® Xpress clinical random access screening platform. The kit is used as an aid in screening pregnant women for pre-eclampsia in all trimesters of pregnancy **and for screening for risk of Down's syndrome in the first trimester of pregnancy.**	Use of the tests for to screen for Down's syndrome, and use of the tests in the first trimester, is outside the scope of this assessment. Therefore, no change has been made to the scope.
		Biochemical marker (PlGF) for screening for risk of pre-eclampsia in the first trimester of pregnancy is used together with risk calculation software (e.g. Preeclampsia Predictor™, **LifeCycle** or other available risk calculation software) in combination with other relevant clinical information. Use of PlGF-based tests for first trimester screening is outside the scope of this assessment.	Use of PlGF-based tests for first trimester screening is outside the scope of this assessment, therefore no further detail on how tests are intended to be used in this manner have been added to the scope.
		Biochemical marker (PlGF) for screening for risk of pre-eclampsia **and for aid in diagnosis of pre-eclampsia and for short term prediction of suspected pre-eclampsia in the second and third trimester of pregnancy together with other biochemical and clinical information.**	Section 2.3 of the scope has been amended to state that: 'In the second and third trimester, the company state that PlGF can be used for screening for risk of pre-eclampsia together with other relevant clinical information'.

		Page 5: **"Using the DELFIA Xpress PlGF 1-2-3 test alone, the process time for first results is 30 minutes. Using both DELFIA Xpress PlGF 1-2-3 and sFlt-1 together takes approximately 31,5 minutes for the first sFlt-1/PlGF ratio result. The instrument is processing several samples simultaneously, leading to approximately 40 results per hour throughput."**	Section 2.2.3, page 4 of the final scope has been amended to state: 'Using the DELFIA Xpress PlGF 1-2-3 test alone, the process time for first results is 30 minutes. Using both DELFIA Xpress PlGF 1-2-3 and sFlt-1 together takes approximately 31,5 minutes for the first sFlt-1/PlGF ratio result. The instrument is able to process samples simultaneously, leading to approximately 40 results per hour throughput'.
		"The company state that the recommended cut-off values for the DELFIA Xpress PlGF 1-2-3 test **alone** are:"	This sentence has been amended as suggested.
		"For aid in diagnosis and for short term prediction of pre-eclampsia, using cut-offs validated in the laboratory, the sFlt-1/PlGF ratio results may be categorized to: **•Ratio below low cut off: rule out** **•Ratio above increased cut off: rule in**"	This section of the final scope has been updated to: 'For aid in diagnosis and for short term prediction of pre-eclampsia, using cut-offs validated in the laboratory, the sFlt-1/PlGF ratio results may be categorized to: • Low (ratio below low cut off): rule out • Intermediate to follow-up • Increased (ratio above increased cut off): rule in'. See section 2.2.3, page 5.
		"The DELFIA Xpress PlGF 1-2-3 assay has a limit of detection of 1.9 picograms/millilitre and a limit of quantitation of 3.3 picograms/millilitre	This sentence has been amended as suggested.

Who	Section	Comment	NICE Response
		(measuring range 1.9 to 4000 picograms/millilitre). The DELFIA Xpress sFlt-1 has a limit of detection of is 3.79 picograms/millilitre and a limit of quantitation of 7.6 picograms/millilitre **(measuring range 3.79 to 19500 picograms/millilitre)**."	
Perkin Elmer	• Can any of the tests be used in a near patient setting (at point of care) in the NHS, or would they need to be done in a laboratory?	All tests need laboratory settings because sample pre-treatment (centrifugation) is required. DELFIA Xpress PlGF 1-2-3 and DELFIA Xpress sFlt-1 kits are required to be used in a laboratory.	Thank you for your comment which we have considered.
Perkin Elmer	• Are each of the technologies in use in the NHS and relevant to the evaluation?	Yes, each of the technologies are relevant to the evaluation.	Thank you for your comment which we have considered.
Perkin Elmer	• Are there any other technologies with a similar purpose in use in the NHS?	No additional than those in this scope.	Thank you for your comment which we have considered.
Perkin Elmer	**Target condition** • How should *suspected* pre-eclampsia be defined?	Patients who do not meet the full criteria of the condition of pre-eclampsia (as described in the NICE hypertension in pregnancy guideline) would be considered to have suspected pre-eclampsia.	Thank you for your comment which we have considered.
Perkin Elmer	• What distinguishes a person with suspected pre-eclampsia and someone with a diagnosis of the condition?	A person suspected of having pre-eclampsia is someone presenting to a healthcare professional who is more than 20 weeks pregnant with either blood pressure >140/90mmHg or complaining of symptoms such as headache, visual disturbances or epigastric/right upper quadrant pain. A diagnosis of pre-eclampsia requires fulfilment of the diagnostic criteria of pre-eclampsia used in the region (ie ISSHP).	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Perkin Elmer	**Care pathway** • If a person has a positive PlGF-based test result for pre-eclampsia, what changes to their care would occur?	Her antenatal care would be tailored based on the severity of their condition. They would likely be hospitalised and commenced on antihypertensive medication. They would have blood tests to monitor the severity of the condition. The fetal well-being would also be assessed. If they are above 37 weeks, they would be either induced or delivered by caesarean section. Prior to 37 weeks, they would be seen more frequently at the hospital and delivered when deemed appropriate taking into consideration both the maternal health and fetal health.	Thank you for your comment which we have considered.
Perkin Elmer	• Under what circumstances would someone have a repeat PlGF-based test if an initial test had been done and was negative?	PlGF < 50pg/ml or sFlt-1/PlGF ratio below laboratory specific lower cut off: • For patients with early onset, consider a follow-up PlGF test 1–2 weeks later, according to the individual clinical situation. PlGF > 150pg/ml or sFlt-1/PlGF ratio above laboratory specific upper cut off: • these women will most likely not develop pre-eclampsia for at least 1 week; therefore, if they are still symptomatic, they will need to be reassessed.	Thank you for your comment which we have considered.
Perkin Elmer	**Population** • Is the population defined appropriately?	Yes	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Perkin Elmer	• Should people with severe hypertension (BP of 160/110 mmHg or more) be excluded from the population for this assessment (because they would be admitted to hospital regardless of their PlGF-based test result)?	No, the PlGF test provides prognosis on the evolution of the pregnancy	Thank you for your comment which we have considered.
Perkin Elmer	• Are there groups within this population that should be considered separately?	No	Thank you for your comment which we have considered.
Perkin Elmer	**Comparator** • Is this the most appropriate comparator for the assessment?	Yes	Thank you for your comment which we have considered.
Perkin Elmer	**Outcomes and costs** • Will these outcome and cost measures capture the most important benefits (and harms) of the technology?	Yes	Thank you for your comment which we have considered.
Perkin Elmer	**Equality** • NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed scope may need changing in order to meet these aims. In particular, please tell us if the proposed scope:		

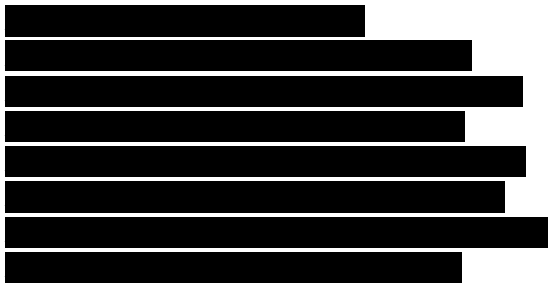
Who	Section	Comment	NICE Response
Perkin Elmer	**Provisional stakeholder list** • Are there any stakeholders who should be invited to participate in the assessment?	[redacted].	Thank you for your comment which we have considered. Individuals are not invited to register as stakeholders.
Perkin Elmer	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.		
Roche	**Introduction/product properties** • Are these sections accurate and complete?		
Roche	**Technologies** • Are the descriptions of the technologies accurate?	Angiogenesis is mentioned for PlGF so anti-angiogenesis should be mentioned for sFlt-1. The data from DG23 and supporting publications show that sFlt-1 is higher in pre-eclampsia, not "thought" to be higher (as the wording for PlGF). The marketing authorisations of each of the tests should be checked. Some tests available on the market are intended to rule out delivery due to pre-eclampsia, rather than aid in diagnosis, for example.	Thank you for your comments which we have considered. Section 2.1, page 1 of the final scope has been amended to: 'In addition, some PlGF-based tests also measure soluble FMS-like tyrosine kinase-1 (sFlt-1), an anti-angiogenic protein…' Section 2.1, page 1 has been amended to: 'the levels of sFlt-1 **may** be higher than those seen in normal pregnancy'.

Who	Section	Comment	NICE Response
Roche	• Can any of the tests be used in a near patient setting (at point of care) in the NHS, or would they need to be done in a laboratory?	The Elecsys sFlt-1 and PlGF are only for use on the automated cobas platforms and are based in the laboratory. Some hospitals are set up so that tests done in a central laboratory can be returned within 1-2 hours. Moreover, though not suitable for NPT, the smaller automated platform cobas e411 (& upcoming new version) is often used in smaller critical care labs/clinic settings e.g for TnT hs and NT-proBNP, potentially enabling faster turnarounds. We would caution against assuming that point of care testing is significantly faster than laboratory testing. The turnaround time of point of care testing strategies may also be limited by workflow backlogs and availability of staff time to manage the equipment.	Thank you for your comment which we have considered.
Roche	• Are each of the technologies in use in the NHS and relevant to the evaluation?		
Roche	• Are there any other technologies with a similar purpose in use in the NHS?		
Roche	**Target condition** • How should *suspected* pre-eclampsia be defined?	As in DG23.	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Roche	• What distinguishes a person with suspected pre-eclampsia and someone with a diagnosis of the condition?	National guidelines for diagnosis should be followed. The sFlt-1/PlGF ratio is intended for use as an aid in the diagnosis of preeclampsia in conjunction with other diagnostic and clinical information.The sFlt-1/PlGF ratio may also help the clinician to differentiate between pre-eclampsia, gestational and essential hypertension, enabling tailored treatment strategies.	Thank you for your comment which we have considered.
Roche	**Care pathway** • If a person has a positive PlGF-based test result for pre-eclampsia, what changes to their care would occur?		
Roche	• Under what circumstances would someone have a repeat PlGF-based test if an initial test had been done and was negative?	The NICE assessment should seek to determine the optimal timing of repeat testing based on the different tests' abilities to rule out pre-eclampsia for 1, 2, 3 or 4 weeks. Recommendations shouldn't preclude retesting where clinically indicated.	Thank you for your comment which we have considered.
Roche	**Population** • Is the population defined appropriately?	Patients with suspected pre-eclampsia in the first trimester should be included in the review as a separate population. There are strong data on the clinical utility of testing. Please see Roche Diagnostics Ltd's response to manufacturer information for a list of references.	Thank you for your comment which we have considered. Use of the tests in the first trimester is outside the scope of this assessment.
Roche	• Should people with severe hypertension (BP of 160/110 mmHg or more) be excluded from the population for this assessment (because they would be admitted to hospital regardless of their PlGF-based test result)?	No. They should be included as a subgroup.	Thank you for your comment which we have considered. Women with severe hypertension (BP of 160/110 mmHg or more) have been included as a sub-group. See section 5 page 15 of the final scope.

Who	Section	Comment	NICE Response
Roche	• Are there groups within this population that should be considered separately?	Twin pregnancies. Renal disease.	Thank you for your comment which we have considered. Women with renal disease and women with multiple pregnancies (for example, twin or triplet pregnancies) have been included as sub-groups in the final scope. See section 5, pages 15 and 16.
Roche	**Comparator** • Is this the most appropriate comparator for the assessment?		
Roche	**Outcomes and costs** • Will these outcome and cost measures capture the most important benefits (and harms) of the technology?	The assessment should also include the costs of unnecessary testing (testing cost during monitoring for patients in the "no pre-eclampsia testing" arm). We would suggest contacting the authors of the INSPIRE trial for a breakdown of cost-savings they collected as part of that trial. They may be willing to provide these data to the EAG. We would highlight the logistical challenges associated with POC tests that we mentioned in section 3 above. We would ask that the negative predictive value of the test to rule-out pre-eclampsia at 1, 2, 3 and 4 weeks are specifically listed as outcomes of interest in the scope.	Thank you for your comments which we have considered. Text has been added to the intermediate outcome 'diagnostic accuracy' in the scope table on page 16 of the final scope to state that this includes positive and negative predictive values.

Who	Section	Comment	NICE Response
Roche	**Equality** • NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed scope may need changing in order to meet these aims. In particular, please tell us if the proposed scope:		
Roche	**Provisional stakeholder list** • Are there any stakeholders who should be invited to participate in the assessment?	We would suggest that the following stakeholders are also included:- • Royal college of cardiologists • Institute of Health Visiting • Maternal Mental Health Alliance • University Hospitals Birmingham	Thank you for your comment which we have considered. Cardiology is a subgroup of the RCP which have registered as a stakeholder. The Institute of Health Visiting and the Maternal Mental Health Alliance will be invited to register as stakeholders. University Hospitals Birmingham could register as part of NHS services but we would not usually invite a specific hospital to register.

Who	Section	Comment	NICE Response
Roche	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.	It may be possible to access provisional data from the PARROT-2 study before the end of the assessment. NICE could seek this data from the investigators and should bear it in mind when making recommendations about repeat testing. 	Thank you for your comment which we have considered.
Thermofisher	**Introduction/product properties** Are these sections accurate and complete?	Require changes to technology sections, see question 2 below.	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Thermofisher	**Technologies** • Are the descriptions of the technologies accurate?	Accurate however to align comparison with other suppliers we suggest the following changes to section 2.2.4, • The BRAHMS PlGF plus Kryptor test can be used stand-alone test or together with BRAHMS sFlt-1 Kryptor • "The assays are indicated for the quantitative determination of sFlt-1 and PlGF in serum samples and are compatible with the BRAHMS Kryptor compact plus analyser" Note **also compatible with Kryptor Gold immunoanalyser** • Using the Kryptor Gold Immunoanalyser, it takes 29 minutes the first BRAHMS sFlt-1 Kryptor / BRAHMS PlGF plus Kryptor ratio result, and then 90 seconds for each additional result	Thank you for your comment which we have considered. This detail has been added to section 2.2.4, page 5 of the final scope. This detail has been added to section 2.2.4, page 5: 'The assays are indicated for the quantitative determination of sFlt-1 and PlGF in serum samples and are compatible with the BRAHMS Kryptor compact plus analyser and the Kryptor Gold immunoanalyser'. This detail has been added to section 2.2.4, page 5 of the final scope: 'When using the Kryptor Gold Immunoanalyser it takes 29 minutes for the first BRAHMS sFlt-1 Kryptor / BRAHMS PlGF plus Kryptor ratio result, and then a further 90 seconds for each additional result'.
Thermofisher	• Can any of the tests be used in a near patient setting (at point of care) in the NHS, or would they need to be done in a laboratory?		

Who	Section	Comment	NICE Response
Thermofisher	• Are each of the technologies in use in the NHS and relevant to the evaluation?	Within the UK NHS (& UK Private Screening Laboratories), the BRAHMS Kryptor immunoanalyser family (Kryptor Compact Plus, Kryptor Gold) are widely in use. BRAHMS Kryptor immunoassays are used for first trimester trisomy screening. The tests are FMF (Fetal Medicine Foundation) approved and are considered the gold standard in prenatal screening throughout the UK NHS and European Health care systems. There are many users throughout the EU of the Kryptor PLGF/sFlt ratio for PE diagnosis. The NHS Innovation and Technology Payment (ITP) program is a very welcome initiative, however, despite much interest, the program limits the ability of non-recommended suppliers to access the NHS.	Thank you for your comment which we have considered.
Thermofisher	• Are there any other technologies with a similar purpose in use in the NHS?		
Thermofisher	**Target condition** • How should *suspected* pre-eclampsia be defined?	As per ISSHP statement (page 7/8)	Thank you for your comment which we have considered.
Thermofisher	• What distinguishes a person with suspected pre-eclampsia and someone with a diagnosis of the condition?	As per NICE hypertension in pregnancy guideline	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Thermofisher	**Care pathway** • If a person has a positive PlGF-based test result for pre-eclampsia, what changes to their care would occur?	This can aid in the diagnosis of pre-eclampsia. Mothers could be offered admission to hospital for surveillance and any interventions needed if there are concerns for the wellbeing of the woman or baby	Thank you for your comment which we have considered.
Thermofisher	• Under what circumstances would someone have a repeat PlGF-based test if an initial test had been done and was negative?	If someone had a worsening or new-onset of signs or symptoms of possible pre-eclampsia.	Thank you for your comment which we have considered.
Thermofisher	**Population** • Is the population defined appropriately?	Yes	Thank you for your comment which we have considered.
Thermofisher	• Should people with severe hypertension (BP of 160/110 mmHg or more) be excluded from the population for this assessment (because they would be admitted to hospital regardless of their PlGF-based test result)?	Yes	Thank you for your comment which we have considered.
Thermofisher	• Are there groups within this population that should be considered separately?		
Thermofisher	**Comparator** • Is this the most appropriate comparator for the assessment?	Yes	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Thermofisher	**Outcomes and costs** • Will these outcome and cost measures capture the most important benefits (and harms) of the technology?	Yes	Thank you for your comment which we have considered.
Thermofisher	**Equality** • NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed scope may need changing in order to meet these aims. In particular, please tell us if the proposed scope:		
Thermofisher	**Provisional stakeholder list** • Are there any stakeholders who should be invited to participate in the assessment?		
Thermofisher	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.		
Quidel Ireland	**Introduction/product properties** Are these sections accurate and complete?	Yes	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Quidel Ireland	**Technologies** • Are the descriptions of the technologies accurate?	Yes	Thank you for your comment which we have considered.
Quidel Ireland	• Can any of the tests be used in a near patient setting (at point of care) in the NHS, or would they need to be done in a laboratory?	Both POC and Laboratory	Thank you for your comment which we have considered.
Quidel Ireland	• Are each of the technologies in use in the NHS and relevant to the evaluation?	Yes	Thank you for your comment which we have considered.
Quidel Ireland	• Are there any other technologies with a similar purpose in use in the NHS?	Yes	Thank you for your comment which we have considered.
Quidel Ireland	**Target condition** • How should *suspected* pre-eclampsia be defined?	As described no comments	Thank you for your comment which we have considered.
Quidel Ireland	• What distinguishes a person with suspected pre-eclampsia and someone with a diagnosis of the condition?	As described no comments	Thank you for your comment which we have considered.
Quidel Ireland	**Care pathway** • If a person has a positive PlGF-based test result for pre-eclampsia, what changes to their care would occur?	As described as an adjunct to exalting clinical pathway	Thank you for your comment which we have considered.
Quidel Ireland	• Under what circumstances would someone have a repeat PlGF-based test if an initial test had been done and was negative?	None	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Quidel Ireland	**Population** • Is the population defined appropriately?	Yes	Thank you for your comment which we have considered.
Quidel Ireland	• Should people with severe hypertension (BP of 160/110 mmHg or more) be excluded from the population for this assessment (because they would be admitted to hospital regardless of their PlGF-based test result)?	No	Thank you for your comment which we have considered.
Quidel Ireland	• Are there groups within this population that should be considered separately?	No	Thank you for your comment which we have considered.
Quidel Ireland	**Comparator** • Is this the most appropriate comparator for the assessment?	Yes	Thank you for your comment which we have considered.
Quidel Ireland	**Outcomes and costs** • Will these outcome and cost measures capture the most important benefits (and harms) of the technology?	Yes	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
Quidel Ireland	**Equality** • NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed scope may need changing in order to meet these aims. In particular, please tell us if the proposed scope:	No comments	Thank you for your comment which we have considered.
Quidel Ireland	**Provisional stakeholder list** • Are there any stakeholders who should be invited to participate in the assessment?	No	Thank you for your comment which we have considered.
Quidel Ireland	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.	No further comments.	Thank you for your comment which we have considered.

Who	Section	Comment	NICE Response
RCOG	**General** • Please tell us if there are any other key points that are important and relevant to consider for this assessment that are not currently included in this draft scope.	• Could the scope clarify if this test is intended to be applicable to women with twin pregnancies?	Thank you for your comments which we have considered. This assessment will consider all pregnant women between 20 weeks and 36 weeks and 6 days of pregnancy who have suspected pre-eclampsia. Women with multiple pregnancies (for example, twin or triplet pregnancies) have been included as a sub-group in the final scope (see section 5, page 16), so any identified data showing the effectiveness of the tests in this group will be presented in the assessment.
		• Is the PLGF result affected by the initiation of anti hypertensive medication - or is the sensitivity & specificity affected by concurrent antihypertensive medication? Worried that might be falsely reassured with treated hypertension.	Use of the tests will be assessed in women with chronic hypertension which will include women who are taking antihypertensive medication, so any impact of antihypertensive medication on test performance will be investigated in this group (dependent on the availability of data).
		• Will further reassessment and retests be accounted for in cost effectiveness analysis?	The use of the interventions will be assessed when used for repeat testing.