Proposal for assessment of new health technologies

Important information – read this first!

- Submitted proposals for national health technologies (HTAs) will be published in full. If the proposer thinks there is information necessary for filling out the form, that should not be made public, please contact the secretariat (Nye Metoder) before submission.

  The proposer is aware that the form will be published in its entirety (tick): ☒

- Proposer has filled out point 19 below «Interests and, if any, conflicts of interest» (tick): ☒
- This form serves the purpose to submit proposals for health technology assessment (HTA) at the national level in Nye Metoder - the national system for managed introduction of new health technologies within the specialist health service in Norway. The form does not apply to proposals for research projects. A health technology assessment is a type of evidence review, and for this to be possible, documentation is required, e.g. from completed clinical trials. Lack of documentation may be one of the reasons why the Commissioning Forum (Bestillerforum RHF) does not assign a health technology assessment.
- If the proposal concerns a medical device, the proposer is familiar with the document «Guidance criteria for management of medical devices in the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway» (link) (tick): ☐

Contact information:

Name of the proposer (organization / institution / company / manufacturer)**:**

DiuVita Diagnostics AS

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Date and locality:

03.10.2019 Krokstadelva, Norge

1. Proposer's title on the proposal: *
   *This may be changed during the course of the process"

EarlyCDT Lung, a blood test for the risk assessment of indeterminate pulmonary nodules

2. Brief description of the health technology proposed to be considered:

EarlyCDT Lung is a blood test that reclassifies the malignancy risk of indeterminate pulmonary nodules. The test is complementary to CT scans and positive results add to the risk score allowing faster intervention

3. Brief description of current standard of care (SOC) (Which health technology (ies) are currently used. What is the status of the technology (ies)? Whether it provides curative treatment, life extension, etc.)
   Will the proposed technology replace or be a supplement to today's SOC?

The current recommendation for the management of IPNs is to consider image-guided biopsy, excision biopsy, or CT surveillance, depending on the views of the clinician and patient. Most patients are placed in CT surveillance in an effort to reduce harms caused by surgical investigation of benign nodules, as most nodules (up to 96%) are not cancerous. CT surveillance provides follow-up CTs at 3, 6, 12 and 24 months. If the nodule volume doubling time is greater than 25%, the patient is then moved into intervention. After 24 months with growth <25% the nodule is assumed to be benign and patient is discharged. This is far from ideal, as patients are left not knowing if they have lung cancer for up to 2 years and the wait runs the risk of allowing a tumour to advance in stage and therefore reducing the likelihood of a favourable outcome for the patient. EarlyCDT Lung is used at the time of initial nodule detection where normally the patient would be placed in CT surveillance. If positive, the patient can be immediately sent for biopsy, rather than waiting for further tumour growth before action is taken. As a rule-in test, those patients that do not have a positive EarlyCDT Lung result remain in CT surveillance to ensure no cancers are missed. EarlyCDT Lung is highly validated and CE marked, making it available for clinical decision making across Europe. It has been marketed in the USA since 2012 with 160,000 tests sold. A health economics study by the University of Leeds Academic Centre for Health Economics concluded that use of EarlyCDT Lung for assessment of risk of IPNs in the UK NHS would generate additional quality adjusted life years (QALY), at a cost of £2,000 per QALY or below.

4. This proposal concerns:

	Yes	No
A brand new and innovative health technology	☒	☐
Anew application, or a new indication for an established method	☐	☐
A comparison between several methods	☐	☐
A technology that is already in use	☐	☐
If yes – technology used in clinical practice	☐	☐

If yes – technology used in research/clinical trials	☐	☐
A re-evaluation of technology used in clinical practice	☐	☐
The technology is relevant for disinvestment	☐	☐

"Please include further details about any use of the technology"

5. This health technology involves (Multiple ticks are possible)

Pharmaceutical	☐
Medical device/IVD medical device that is CE-marked*	☒

There are two intended uses as part of the CE mark:

1. Primary screen of human patients at high risk of lung cancer:

   ≥50 years of age with at least a 20 pack year smoking history

   40-49 years of age with at least a 20 pack year history plus at least one additional risk factor.

2. Reflex test on human patients to further assess the risk of lung cancer being present where indeterminate lung nodules have been detected but have not been diagnosed as malignant.

This application concerns the second intended use above.

Medical device/IVD medical device that is not CE-marked	☐
Procedure	☐
Screening	☐
Highly specialized services / national offers	☐
Organization of the health services	☐
Other (describe)	☐

"If relevant, please include who should be responsible for developing the technology."

6. Application of the technology:

Prevention	☐
Assessment and diagnostics	☒
Treatment	☐
Rehabilitation	☐
Specialist health care	☐
Primary health care	☐

"Please give a description here"

7. Responsibility for funding

	Yes	No
Is the specialized health service responsible for financing the technology today?	☐	☒
May the specialized health service become responsible for funding the health technology?	☒	☐

EarlyCDT Lung is a novel test that is not currently reimbursed by the Norwegian health system. Funding for the test should be from the source that would normally fund the cost of follow up CT scans for patient with IPNs.

8. Is the technology mentioned in the national guidelines or action programs prepared by the Norwegian Directorate of Health?

Yes	No
☐	☒

EarlyCDT Lung fits into the guidelines published by the various bodies, such as the British Thoracic Society Guidelines for the Management of Pulmonary Nodules. EarlyCDT Lung simply slots into the pathway at the point at which CT surveillance is considered. If the test is positive, patients then flow into the intervention pathway. Otherwise they remain on the pathway for CT surveillance.

9. Does the technology involve the use of radiation (ionizing/ non- ionizing)?

Yes	No
☐	☒

"Give a short description of type of radiation source, device and degree of radiation exposure"

10. Which discipline(s) does the health technology apply to, and which patients are affected? (Could the health technology also affect other groups (e.g. health personnel or relatives)?)

The test is applied by pulmonologists in support of their assessment of lung health patients.

11. Which aspects are relevant to the assessment? (Multiple ticks are possible)

Clinical efficacy	☒
Safety/adverse effects	☐
Costs/resource use	☒
Cost-effectiveness	☒
Organizational consequences	☒
Ethical	☐
Legal	☐

12. Please suggest the main scope/objective for the health technology assessment, as well as secondary scopes/objectives (in compliance with question 10). For those familiar with "PICO" (Patient, Intervention, Comparator, Outcome) – please include tentative suggestions for PICO.

The objective of the health technology assessment should be to compare the use of EarlyCDT Lung against the standard of care (CT surveillance) to assess the potential for improvements to patient care, lives saved from earlier intervention and costs to the health system.

Population:

Patients identified with a pulmonary nodule by CT or chest x-ray where the risk of malignancy is between 10% and 70%. Patients can be identified by low dose CT for lung cancer screening, or incidentally during investigations of other diseases.

Intervention:

Prior to placing a nodule patient in CT surveillance apply EarlyCDT-Lung, and:

For Intermediate risk IPNs consider intervening if pretest risk is >10% and EarlyCDT—Lung is High, or consider intervening if pretest risk is >27.5% and the test is Moderate. Do not change the pre-test planned clinical management if the test result is No Significant Level of Autoantibodies Detected.

Comparator:

CT surveillance, with CT scans at 3, 6, 12 and 24 months. If nodule volume doubling time (VDT) >25%, further intervention is recommended. If the nodule VDT <25% after 2 years, the patient is discharged.

Outcomes:

Patients are moved to intervention faster if their EarlyCDT Lung test is positive

A survey in the USA showed that, fewer harms would be recorded as clinicians would perform fewer interventions on false positives, but importantly, no patients would be removed from CT surveillance if the test result was No Significant Level of Autoantibodies Detected.

In a study performed By University of Leeds, funded by the UK NHS, EarlyCDT Lung was found to be cost-effective compared to CT surveillance with an incremental cost-effectiveness ratio (ICER) of less than £2,500.

13. Please give a brief explanation of why it is important that the health technology assessment proposed should be conducted.

EarlyCDT Lung assessment of risk of IPNs results in a higher number of QALYs compared to CT surveillance alone. It also reduces anxiety and reduces the uncertainty in the management of IPNs.

The health economics in the UK have been studied by the University of Leeds and this model can be adjusted for the Norwegian market to allow assessment of the impact in this country.

A HTA on EarlyCDT Lung will help drive adoption and reimbursement discussions in the public healthcare system, therefore improving patient management and outcomes.

14. Please comment on the technology that is proposed to be assessed with regard to the following points:

The severity of the disease/condition the health technology targets

Lung cancer has poor outcomes due to the late stage at which the disease is usually detected. In Norway there are 3,200 lung cancers per year and 2,200 deaths. Lung cancer causes 21% of all cancer deaths in the country.

A key to improving outcomes is early diagnosis and intervention. When treated at stage 1, survival is over 80%. At stage 4 it is below 20%.

As a high specificity test, EarlyCDT Lung ensures that the clinician can intervene confidently without causing harm due to overtreatment of benign diseases.

Expected effect

Early intervention by EarlyCDT Lung will reduce the time from referral to treatment, save on Follow up CT scans and reduce patient anxiety caused by waiting.

Safety

EarlyCDT Lung has been validated in >120,000 patient samples and recently completed a 12,208 person trial in Scotland, which demonstrated a 36% reduction in late stage lung cancer presentations.

EarlyCDT Lung is a simple blood test and therefore the only harms caused from taking the test itself are those of drawing blood.

The test is high specificity, moderate sensitivity and so used as a rule-in test. The positive predictive value of EarlyCDT Lung when applied to IPNs is 70%. As such, 3 in 10 patients moved into intervention will have benign disease. This should be balanced against a poorer PPV in the current handling of IPNs, where a high number of interventions are in benign disease and a number of patients that remain in CT surveillance risk an increase in stage before the cancer is diagnosed. In a US study, 22% of patients progressed in stage in under 60 days. This time is less than the recall frequency in CT surveillance.

It is currently regulated in the EU as a self-certified IVD test. Under the new IVD regulations, EarlyCDT Lung will become a Class C IVD test.

Total number of patients in Norway the health technology is applicable to

Exact figures are unknown. However, nodule prevalence in high risk populations (smokers) is approximately 13%. In CT screened populations (very high risk), it can be as high as 33%.

Consequences for resource use in the public health service

EarlyCDT Lung use for IPN assessment will reduce the follow-on CTs in 10% of the patients receiving the test, as they will move to intervention without further CTs. This will reduce CT scanner demand and radiologist time required.

There will be an impact in increasing the number of interventions as that 10% would require PET-CT, or biopsy.

EarlyCDT Lung implementation does not save money in the health service as a whole, but is highly cost effective at under 30,000NOK

Need for revision of existing national guidelines or preparation of new guidelines

The revision would be to place EarlyCDT Lung in the pathway at the point where the clinician is considering placing the patient in CT surveillance. Prior to placing a nodule patient in CT surveillance apply EarlyCDT-Lung, and: For Intermediate risk IPNs consider intervening if pretest risk is >10% and EarlyCDT—Lung is High, or consider intervening if pretest risk is >27.5% and the test is Moderate. Do not change the pre-test planned clinical management if the test result is No Significant Level of Autoantibodies Detected.

15. Please provide references to documentation of the health technology's effect and safety (i.e. previous technology assessments). (Up to 10 key references can be provided, please do not send attachments in this step of the process):

Sutton AJ, et al Cost-effectiveness of a new autoantibody test compared to computed tomography (CT) surveillance in the diagnosis of lung cancer amongst patients with indeterminate pulmonary nodules. (Submitted)

Edelsberg J, et al Cost-effectiveness of an autoantibody test (EarlyCDT-Lung) as an aid to early diagnosis of lung cancer in patients with incidentally detected pulmonary nodules. PLoS One. 2018;13(5):e0197826. doi: 10.1371/journal.pone.0197826

Sullivan FM, et al Detection in blood of autoantibodies to tumour antigens as a case-finding method in lung cancer using the EarlyCDT®-Lung Test (ECLS): study protocol for a randomized controlled trial BMC Cancer volume 17, Article number: 187 (2017)

Healey GF, et al Tumor-Associated Autoantibodies: Re-Optimization of EarlyCDT-Lung Diagnostic Performance and Its Application to Indeterminate Pulmonary Nodules. JCT 2017 Vol.8 No.5 DOI: 10.4236/jct.2017.8504

Jett JR, et al. Audit of the autoantibody test, EarlyCDT®-lung, in 1600 patients: an evaluation of its performance in routine clinical practice. Lung Cancer. 2014 Jan;83(1):51-5. doi: 10.1016/j.lungcan.2013.10.008

Healey GF, et al. Signal stratification of autoantibody levels in serum samples and its application to the early detection of lung cancer J Thorac Dis. 2013 Oct; 5(5): 618–625. doi: 10.3978/j.issn.2072-1439.2013.08.65

Chapman CJ, et al. EarlyCDT®-Lung test: improved clinical utility through additional autoantibody assays. Tumour Biol. 2012 Oct;33(5):1319-26. doi: 10.1007/s13277-012-0379-2.

Lam S, et al. EarlyCDT-Lung: an immunobiomarker test as an aid to early detection of lung cancer. Cancer Prev Res (Phila). 2011 Jul;4(7):1126-34. doi: 10.1158/1940-6207.CAPR-10-0328.

Chapman CJ, et al Immunobiomarkers in small cell lung cancer: potential early cancer signals. Clin Cancer Res. 2011 Mar 15;17(6):1474-80. doi: 10.1158/1078-0432.CCR-10-1363.

Boyle P, et al. Clinical validation of an autoantibody test for lung cancer. Ann Oncol. 2011 Feb; 22(2): 383–389. doi: 10.1093/annonc/mdq361

Murray A, et al. Technical validation of an autoantibody test for lung cancer. Ann Oncol. 2010 Aug; 21(8): 1687–1693. doi: 10.1093/annonc/mdp606

Chapman CJ, et al. Autoantibodies in lung cancer: possibilities for early detection and subsequent cure. Thorax. 2008 Mar;63(3):228-33.

16. Please provide the name of the marketing authorization holder/manufacturer/supplier of the health technology (if applicable/available):

Oncimmune Limited

17. Marketing Authorization Status (MA) or CE-marking: When is MA or CE- marking expected? If possible, provide the time of planned marketing:

CE marked 31/05/2017

18. Additional relevant information (up to 300 words.)

"Click in the field and type"

19. Interests and potential conflicts of interests

Please describe the proposer's relationships or activities that may affect, be influenced by, or be perceived by others to be important for further management of the health technology that is proposed assessed. (E.g. proposer has financial interests in the matter. Proposer has or has had assignments in connection with the technology or to other actors with interest in the technology)

The proposer (DiuVita Diagnostics AS) has no conflict of interests, we are a distributer company operating in Norway without any influence for the technique or management.