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Draft Preferred Product Characteristics for cellulitis

Intended Purpose:	Aid in the diagnosis of cellulitis.
Rationale	• Misdiagnosis of cellulitis is recognized as a common problem across primary and secondary care services. This contributes both to unnecessary antibiotic use, and missed opportunities for management of alternative diagnoses. • The ideal technology would provide diagnostic support with novel information that would feed into a holistic clinical assessment for diagnosing (or excluding) cellulitis. • From a patient perspective, a technology that can rapidly exclude/confirm cellulitis is the primary priority as this would ideally lead to prompt management and resolution. • From a clinician perspective, a technology that provides information to increase confidence in excluding/confirming bacterial infection would empower clinicians to prescribe antibiotics prudently and stop antibiotics if inappropriately prescribed.
Further Notes for Consideration	• Alongside confirming/excluding bacterial infection, the ideal diagnostic technology would provide information on the severity of infection, allowing for appropriate triage/(de)escalation of patient management. • Misdiagnosis is in part related to a lack of agreement on what constitutes cellulitis. Cellulitis can be restricted to non-purulent cases, or expand to include purulence, wounds, abscesses and exist on a continuum with erysipelas and necrotising fasciitis. An ideal diagnostic technology should clearly identify whether it addresses the restricted, expanded or both definitions of cellulitis.
Glossary	**Primary care**: First point of contact in the healthcare system, including general practice, community pharmacy, dentistry, eyecare [https://digital.nhs.uk/developer/guides-and-documentation/introduction-to-healthcare-technology/the-healthcare-ecosystem] **Secondary care**: Hospital, emergency and mental health care.

[https://digital.nhs.uk/developer/guides-and-documentation/introduction-to-healthcare-technology/the-healthcare-ecosystem]

Holistic clinical assessment: Evaluating patients using a wide range of information e.g. physical examination, tests and measurements, patient history, social circumstances, psychological needs, for personalised care.

Triage: "A way of deciding the urgency of a person's need for support or medical treatment."

[https://thinklocalactpersonal.org.uk/jargon-buster/]

(De)Escalation (of patient management): Lowering or raising the intensity or concern level associated with a patient's treatment.

Purulence: Containing or producing pus

Abscess: Collection of pus

[https://patient.info/infections/abscess-leaflet]

Erysipelas: Infection of the upper layers of the skin, a less serious version of cellulitis

[https://patient.info/skin-conditions/skin-rashes/cellulitis-and-erysipelas]

Necrotising fasciitis: Uncommon, life-threatening infection involving deep layers of skin and the underlying body area beneath the affected skin. [https://www.nhs.uk/conditions/necrotising-fasciitis/]

Target Population: Adults and children presenting with lower limb cellulitis.

Rationale

- The leg is the most common site of cellulitis infection.
- Research on the misdiagnosis rate across sites of infection and the range of alternative diagnoses in adult cellulitis suggest the lower limb is a very common, if not the most common, site of misdiagnosis.
- The greatest value of a diagnostic technology is in supporting diagnosis where there is high clinical uncertainty. This occurs particularly in the older adult population among whom clinical mimics of lower limb cellulitis are more common and cellulitis may present atypically in the context of different co-morbidities e.g. obesity, heart failure etc.
- Cellulitis may be particularly difficult to diagnose in people with black or brown skin since the clinical diagnosis relies on identification of erythema.

	• People experiencing homelessness and people who inject drugs are also at high risk of cellulitis and often have chronic, skin and soft tissue changes related to trauma and infection which make acute intercurrent cellulitis difficult to diagnose. • Lower limb cellulitis occurs in adults and children and a diagnostic technology of value in adults would also be expected to be of value in children.
Further Notes for Consideration	• A technology that has been validated for lower limb cellulitis could be further validated for other sites of infection, allowing for a broader scope of use. • Additional sites to prioritise following validation in the lower limbs include the upper limbs and facial/orbital cellulitis. Upper limb cellulitis is relevant particularly for lymphoedema patients and working-age men secondary to trauma. For the paediatric population, cellulitis in the facial/orbital region is related to risk of hospital admission.
Glossary	**Co-morbidities:** Having multiple health conditions at the same time. **Clinical mimics**: Health conditions that look like cellulitis. **Erythema**: Redness of skin **Intercurrent**: Having a new illness/health condition while another illness/condition is ongoing.

Intended user and use setting:	Appropriately trained staff in first contact encounters, which may include but is not limited to: medical, nursing, pharmacy and nursing/care-home staff.
Rationale	• People with cellulitis present to a wide range of locations from patient's own homes in district nursing, care/nursing homes, commercial pharmacies, GP practices, emergency departments and urgent treatment centres. • Getting diagnosis right at first contact encounters presents the largest opportunity for healthcare savings and reduced patient suffering. • Given the wide range of first contact encounter settings, different staffing groups may be appropriately trained to use the health technology to

	obtain and escalate the results, which is distinct from interpretation and clinical decision-making regarding the results.
Further Notes for Consideration	• Use of the technology may be separated from clinical decision-making, i.e. the person using the technology need not be the person making the diagnosis or management decision, but a clinical pathway must exist for the output to be reviewed by appropriate clinical staff. • Provided the diagnostic technology is established across first contact settings, a secondary scope could be direct patient use. However, a care pathway and established patient-clinician relationship should exist to facilitate appropriate and timely communication, clinical decision-making and management of the patient-obtained results.
Glossary	**First contact encounter**: The first time patient seeks help from health and care services for a particular health problem.

Modality:	Recognising no single medical device modality, currently in use, is a definitive forerunner for a cellulitis diagnostic technology, the modality may be: • Imaging based. Technologies, such as, but not limited to: spectroscopy, fluorescence, point-of-care ultrasound, thermal imaging, non-contact infrared thermometer, in which level of invasiveness is limited maximally to surface contact. • Blood based. Venous/capillary blood samples taken peripherally and not from the site of infection. • Combined. Utilising 2 or more modalities e.g. blood test and imaging test used together.
Rationale	• Imaging modalities have shown promise as diagnostic aids in small-scale studies for cellulitis. However, none are currently in use as standard practice in either secondary or primary care. • Existing in vitro tests e.g. blood culture, tissue biopsy, fine-needle aspiration, DNase B/ASO antibodies, non-specific inflammatory markers have marginal diagnostic value for cellulitis. However, the research into novel biomarkers for cellulitis is limited. As new diagnostic techniques evolve, viable in vitro markers may be identified.

	• Combined approaches may fulfil cost specifications, maximise diagnostic accuracy and clinical effectiveness, while providing complementary information e.g. blood based diagnostic with imaging for spatial extent of infection. • Patients would not find invasive sampling from the site of infection acceptable. Surface contact may be acceptable, provided this leads to a rapid diagnosis and management decision. • For children and young people, diagnostic modalities that are non-invasive and pain-free are preferable to clinicians, parents and patients.
Further Notes for Consideration	Novel modalities may be developed which do not fit the above categories but show promise for diagnosing cellulitis. These should ideally fulfil the other preferred characteristics for this PPC, in particular the access and affordability characteristics (see below).
Glossary	**Medical device**: "Equipment used to diagnose, prevent or treat illness or look after people's health" [https://thinklocalactpersonal.org.uk/jargon-buster/] **Modality**: method or way of doing something. **Spectroscopy**: Study of how light interacts with things. [https://www.britannica.com/science/spectroscopy] **Fluorescence**: When light is released by something after taking in energy. [https://www.britannica.com/science/fluorescence] **Point-of-care**: Tests conducted close to or at the place where patients receive care. [https://www.ncbi.nlm.nih.gov/books/NBK592387/] **Ultrasound**: Method of imaging the inner body using soundwaves. [https://www.nhs.uk/tests-and-treatments/ultrasound-scan/] **Thermal imaging**: Method of imaging using heat released from things. [https://www.oxfordreference.com/display/10.1093/oi/authority.20110803103901232] **In vitro test:** Test that uses samples from the human body e.g. blood or tissue. [https://www.gov.uk/government/publications/in-vitro-diagnostic-medical-devices-guidance-on-legislation] **Tissue biopsy**: "Small sample of skin, tissue or cells taken from your body for testing".

[https://www.nhs.uk/tests-and-treatments/biopsy/]

Fine-needle aspiration: Method of taking body samples using a needle

[https://www.nhs.uk/tests-and-treatments/biopsy/]

DNase B/ASO antibodies: Small proteins produced by the body to defend against Group A streptococcus bacterial infection.

[https://pathology.royalcornwallhospitals.nhs.uk/viewTest.php?ID=496]

Inflammatory markers: Proteins produced by the body during inflammation.

[https://patient.info/treatment-medication/blood-tests/blood-tests-to-detect-inflammation]

Diagnostic accuracy: Measurements of how well a test can identify people who do and people who do not have a health condition.

Clinical effectiveness: "Measure of overall quality of health care that patients receive."

[https://thinklocalactpersonal.org.uk/jargon-buster/]

Clinical Efficacy and Endpoint:	• Diagnostic cellulitis technology should, integrated into holistic clinical assessment, achieve higher diagnostic performance than clinical assessment alone. • The output of the technology may be qualitative (e.g. definitive yes, definitive no, borderline/uncertain – requires further investigation) or quantitative, but should provide information on the degree of uncertainty associated with the result. • The primary clinical endpoint is appropriate management following confirmation/exclusion of cellulitis. • A novel diagnostic should perform as well in improving diagnostic accuracy in people with black or brown skin.
Rationale	• There is currently no reference standard diagnostic test. • Two systematic reviews and meta-analyses of cellulitis misdiagnosis report 39% (95%CI: 31-47%) and 41% (95%CI: 28-56%) of cellulitis diagnoses are incorrect. [DOI: 10.1007/s11606-023-08229-w; DOI:10.1002/jhm.12977]

	• The regulatory framework for medical devices and in vitro diagnostics in the UK and EU requires new technology to meet, if not exceed, the existing standards of clinical performance where the technology will be implemented. • Technology results with gradations enable clinicians to integrate the result within their decision-making with an appropriate level of confidence. • The value of a diagnostic technology is not simply higher diagnostic performance but the clinical impact of this improved performance, which would include rapid appropriate antibiotic therapy, reduced healthcare usage and improved antibiotic stewardship.
Further Notes for Consideration	• Output on the severity of infection is an important secondary characteristic as this could inform treatment escalation decisions. • Depending on modality, serial use of the diagnostic technology within the acute phase of infection may be an approach to increase confidence in the result and/or may provide information on the severity of infection and/or about response to treatment. • Results placed within an appropriately designed and validated algorithm could be a method for achieving higher diagnostic accuracy and/or output on severity of infection. • Research on how clinicians integrate point-of-care test (POCT) results into decision-making indicates test accuracy alone is insufficient and clinician decision-making is highly contextual. Evaluating the integration of cellulitis diagnostic technology into existing practice would provide insight on optimal implementation approaches.
Glossary	**Diagnostic performance**: How well something diagnoses a condition. **Reference standard**: Benchmark used to compare how well other tests perform [https://htaglossary.net/reference-standard] **Systematic Review:** Method that answers a research question by searching and reviewing published studies using a systematic approach to summarise their findings together. [https://www.nice.org.uk/Glossary] **Meta-analysis:** Method to combine the results of several studies looking at the same test or treatment or intervention in order to estimate the overall effect. [https://www.nice.org.uk/Glossary] **Regulatory framework**: Set of laws, guidelines and processes that ensures a minimum standard is reached. [https://www.gov.uk/guidance/regulating-medical-devices-in-the-uk]

Gradation: showing measurement of small differences

Antibiotic stewardship: Managing the careful use of antibiotics across the health and care system to make sure antibiotics will still work in the future.

[https://www.nhs.uk/medicines/antibiotics/antibiotic-antimicrobial-resistance/; https://bnf.nice.org.uk/medicines-guidance/antimicrobial-stewardship/]

Safety:	• The diagnostic technology must meet regulatory requirements for medical devices (e.g. UKCA - UK Medical Devices Regulation), including requirements pertaining to in vitro diagnostics, if relevant to the modality. • Dependant on modality, the technology may have reusable or single-use parts, or a combination. The reusable parts must be compatible with recognised Infection Prevention and Control (IPC) surface disinfection products e.g. Virkon, Chloros, Clinell Wipes. The single use components must be designed for safe disposal after use across intended settings, which include non-clinical environments. • IPC risks associated with implementation of the diagnostic technology should be assessed and managed across intended use settings, which include non-clinical environments. • External Quality Assurance (QA)/Quality Control (QC) should be available for local staff to perform within their local workplace settings.
Rationale	• Developers of a novel diagnostic technology should ideally engage with a regulatory strategy early in the development process as this includes a safety risk assessment and ensures the technology is viable from a regulatory perspective. • Group A streptococcus is one of the primary causative bacteria in cellulitis and is highly infectious. • Technology with QA/QC processes which are complex and/or require the specialist input are less likely to be feasible for implementation across the intended use settings where patients with cellulitis present.

Further Notes for Consideration	• The ideal diagnostic technology should evaluate patient and clinician adverse events, and patient adverse outcomes due to false positives/negatives within its diagnostic accuracy studies, including whether risk of adverse events and adverse outcomes are related to level of clinician experience with the diagnostic technology.
Glossary	**EQA/QC**: Processes that ensure products or services meet necessary quality requirements [https://htaglossary.net/quality-assurance] **Adverse event**: "When something happens that isn't planned and causes harm or puts people at risk of harm" [https://thinklocalactpersonal.org.uk/jargon-buster/] **False positive**: When a test says you have a health condition but actually you don't. **False negative**: When a test says you don't have a health condition but actually you do.

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Delivery Strategy:	• The diagnostic technology is ideally deployable in different settings. Examples include but are not limited to: in-person GP consultation, district nursing home visit, Pharmacy consultation, first presentation at emergency department or urgent treatment centre. • To facilitate real-world implementation, the diagnostic technology should ideally produce results within the time period of a single consultation in these settings, including any assembly of parts, patient preparation required for the technology and time from power-on to ready-to-operate status. • If technology use and primary clinical endpoint are separated in implementation, there must be a pathway to facilitate the timely interpretation and actioning of result (i.e. clinical decision on treatment). • Training on correct technology use, output interpretation and integration within existing workflows, should be designed and implemented for intended users and use settings, prior to deployment of the diagnostic technology.
Rationale	• Process evaluations of clinical trials for POCT in primary care demonstrate poor uptake by clinicians if results take longer than a standard consultation or if the tests disrupt existing consultation workflows. • In some first contact settings the care pathway could be modified to allow the test to be performed in advance, with the result available in time for clinical review, and in consequence, the time to result could be longer. However, in order for the diagnostic to be used in consultations in patient's homes/care home settings it will need to provide a result within the time of the patient contact. • Separating technology use from clinical decision-making without appropriate infrastructure to link diagnostic performance to a primary clinical endpoint presents additional risks to patients. • Ensuring patients with cellulitis are on the right clinical pathway is a priority identified by clinicians. • Studies of POCT implementation support the integration of training prior to real-world test use.
Further Notes for Consideration	• Evidence of clinical and cost-effectiveness would support consideration of the diagnostic technology for inclusion into standard practice.

	• An understanding of the training requirements to achieve expected levels of diagnostic performance would support real-world implementation.
Glossary	**Real-world implementation**: Process of putting something into practice in reality rather than in a research study. **Process evaluation**: Study of how complex interventions work. [https://www.gov.uk/guidance/evaluation-in-health-and-wellbeing-process] **Clinical Trial:** "Scientific study that looks at a specific type of treatment to work out whether it is safe, whether it works and whether it is better than other treatments." [https://thinklocalactpersonal.org.uk/jargon-buster/] **Cost-effectiveness**: **"**A comparison of how much something costs in relation to how much benefit is gained from it." [https://thinklocalactpersonal.org.uk/jargon-buster/]

Power, Connectivity, Environmental factors:	• The diagnostic technology must be compatible with standard mains electricity supplies and should ideally have built-in capacity for autonomous operation through battery power. • Charging capacity across a range of power sources e.g. mains electricity, in-vehicle charging, etc. is desirable. • Time from powering on the technology to clinical use on a patient should be integrable within existing consultation times (please see preferred characteristic: Intended User and Use Setting, and preferred characteristic: Delivery Strategy). • It should incorporate local data storage capacity, with wired/wireless connectivity compatible with international standards, including standards for data security. • If designed for use with software, the software must facilitate Laboratory Information Management System (LIMS) and Electronic Patient Record (EPR) integration or must be compatible with middleware software solutions for LIMS and EPR integration. • The device must retain performance across a reasonable range of temperatures/humidity.
Rationale	• Technology requiring an independent, specialised power supply or time longer than an average consultation for powering-on and ready-to-operate status is unlikely to be feasible in first contact encounter settings. • Point-of-care use may include remote and rural settings where access to care is limited and environmental conditions are variable. • Integration with existing digital healthcare infrastructure is essential for uptake and appropriate patient care.
Further Notes for Consideration	[None]
Glossary	[None]

Presentation:	• From removal of external packaging, the diagnostic technology should ideally not require assembly prior to clinical use. The average time to prepare the technology for operation/pack the technology for storage should be integrable to existing clinical workflows. • Dependant on modality, the technology may have single use parts which require attachment/assembly between patient use. The attachment/assembly should not require further tools or significantly increase the likelihood of user error. • The composition of single use parts and external packaging, and any hazardous waste that may arise from using the technology must allow for safe disposal within existing waste management frameworks, such as the NHS Health Technical Memorandum 07-01. • The technology should be lightweight, portable without specialist equipment by a single individual across the range of intended users (see preferred characteristic: Intended user and use setting), from within a car (European minimum B or C-segment passenger cars/Euro NCAP "small family car"/US compact car) to the intended use setting. • Dimensions that allow for handheld use or storage within a single clinician bag are preferred.
Rationale	• (Dis)assembly/transport without specialist equipment for and lightweight, portable design increase feasibility of implementation and uptake in first contact encounter settings with the populations which present the greatest diagnostic challenge. • High likelihood of user error during assembly may generate safety risks to patients and users, which would negatively impact the acceptability of a new health technology. • Technology whose waste products do not conform with best practices for healthcare waste management are unlikely to be implemented.
Further Notes for Consideration	Characteristics pertaining to first powering of the technology can be found under preferred characteristics: Power, Connectivity, Environmental.

Glossary	[None]

Technical guidance:	• The diagnostic technology should be accompanied by technical guidance on its use, maintenance and troubleshooting, which does not rely on specialised technical expertise to understand or follow. • Guidance on the interpretation of results must be available, independent of any training provided through local delivery strategies. • Information on the potential risks to patients through use of the technology must be included, • Guidance on EQA/QC processes to be performed by local staff must be included.
Rationale	• Providing guidance supports uptake and reduces risk of human error in real-world implementation. • The potential differential diagnoses for cellulitis differ depending on multiple factors such as age and gender, skin pigmentation, and the location of cellulitis infection.
Further Notes for Consideration	[None]
Glossary	[None]

Access and affordability:	• The health technology should be easy to use in primary care and community settings, such that implementation in existing workflows is cost-effective. • The cost of the health technology and its use should be affordable relative to the cost of misdiagnosis at first contact and the subsequent downstream related costs.
Rationale	Cost effectiveness is an essential criterion for implementation in standard practice and in community settings.
Further Notes for Consideration	Ensuring equitable access to the diagnostic technology across population subgroups is an area for future research.
Glossary	[None]