Fractional Exhaled Nitric Oxide (FeNO) Guidance for Primary Care

Guidance development
This guidance has been compiled from contributions from across the South West region to support the introduction and subsequent delivery of the use of FeNO in the primary care setting.

What is Fractional Exhaled Nitric Oxide (FeNO)?
A FeNO device is a small hand-held machine which can be used to measure the fractional expired Nitric Oxide (FeNO) levels in a single expired breath and provides an indication of the eosinophilic inflammation in the airways. FeNO measurement is not considered an aerosol generating procedure and it rarely induces cough. Alongside a detailed clinical history, examination and other important tests to assess variability (peak flow, reversibility and challenge tests) it can be used to support the diagnosis of asthma. A positive test increases the probability of asthma, but a negative test does not exclude asthma (PCRS, 2021). NICE guidance (2019) regards a positive FeNO level of 40 parts per billion (ppb) in adults and 35ppb in children. FeNO only forms one element of the diagnostic process for respiratory diseases and should not be the sole basis of any diagnosis. Commencing any treatment, for example inhalers or onward referral should never be delayed due to lack of or access to FeNO testing.

Why use FeNO testing?
NHS Primary Care Services are being asked to restore asthma registers and monitoring for adults and children, to pre-pandemic levels in 2022/23, as outlined in the Quality and Outcomes Framework (QOF). In addition to spirometry, FeNO can be used to support the diagnosis of asthma, as one of the minimum of two diagnostic tests required by QOF to confirm an asthma diagnosis and for that individual to be added to the asthma register. The National Institute for Health and Care Excellence (NICE), supports the use of FeNO testing alongside clinical assessment, spirometry and peak flow as part of the diagnostic algorithm for adults with respiratory symptoms suggestive of asthma (NICE, 2019). Along with the British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS-SIGN, 2019) both support the use of FeNO as part of an assessment process where asthma is considered possible.

Infection Protection Control considerations.
NHS organisations should ensure a consistent application of all current Infection Protection Control (IPC) measures, following both local and national guidance, and be able to provide assurance on their adherence. This would include room ventilation, social distancing, hand hygiene, environmental cleanliness and use of appropriate Personal Protective Equipment (PPE). Check for the latest nationally available Coronavirus (Covid-19) updates and guidance and liaise directly with your local IPC lead for support in applying the guidance. Each test requires the appropriate filtered mouthpiece. The mouthpiece can be used by the same individual for more than one attempt at testing on the same day but a new mouthpiece is required for each visit.

Which FeNO machine to purchase?
There are currently two NICE approved suppliers of FeNO testing equipment in the UK. There is slight variation between the makes of each machine therefore it is essential that before purchased the specific needs of the equipment within your specific setting/environment is carefully considered. As a minimum the following parameters should be included when making the decision:

- Initial cost of equipment
- Annual cost of contract and/or servicing
- Need for software updates
- On-going cost of consumables including mouthpieces, filters, test cassettes etc, also consider basic cost, bulk-buy, shelf-life
- Functionality including: Adult v Child suitability, screen visibility, visual & audible prompts
- Data storage capacity
- Power source: Charging times and battery life
- Extras: protective carry case, ease of cleaning.

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Familiarising yourself with FeNO devices?
Due to the slight variation between the makes of each machine it is essential that before use those who are performing the FeNO test familiarises themselves with the specific product and model that they will be using. Instruction manuals and How-to-guides can be found on the suppliers’ websites (see additional resources section for links).

Training and Competence
FeNO should be used as an additional tool to support the diagnosis of asthma by clinicians who are trained, confident and competent in the diagnosis of asthma. Training can be accessed as on-line modules via E-learning for health and an additional primary care delivery toolkit is available via the Wessex AHSN website. (see additional resources section for links)
To assure that a clinician is deemed competent to perform quality assured FeNO testing in primary care, this training and the acquired knowledge and skills attained should be assured by completion of an agreed competency framework. (see appendix 1 for: example competency template)

When to undertake FeNO testing – inclusion criteria
- New presentation with intermediate probability of asthma (BTS-SIGN 2019)
- New high probability of asthma - where if resources allow for this to be done without delay prior to commencing treatment (BTS-SIGN, 2019, NICE 2017)
- Complex asthma patients e.g. those not improving with treatment, possible poor compliance to medication and ongoing symptoms. These presentations should all be discussed with a respiratory lead nurse or GP prior to FeNO testing.

The following scenarios may also benefit from FeNO testing:
- To assist in assessing the aetiology of respiratory symptoms
- To help identify the eosinophilic asthma phenotype
- To assess potential response or failure to respond to anti-inflammatory agents
- To establish a baseline FeNO during clinical stability for subsequent monitoring
- To monitor step-down/step-up dosing, or discontinuation of anti-inflammatory medications
- To assist in the evaluation of adherence to anti-inflammatory medications
- Non-compliant patients where FeNO may be used as educational tool

When not to undertake FeNO testing – exclusion criteria
- Children aged 5 or under, or those unable to provide a sustained 6-second blow
- Those presenting with signs of viral infections such as Covid-19, flu, cold-virus
- Those presentation with signs of an infective exacerbation such as a bacterial chest infection

Prioritising FeNO testing
In light of the respiratory diagnostic backlog generated from the Covid-19 pandemic the following considerations should be applied in order to pragmatically prioritise individuals where FeNO testing will likely lead to a change or amendment of their respiratory care management. These might include those who are:
- Suspected of having symptomatic asthma
- Symptomatic, but not clear, where the clinician is considering increasing treatment
- Stable but clear, where the clinician is considering step-down treatment
- Non-compliant, where FeNO may be used as educational tool

Also:
- Those identified as most likely to require a referral for severe asthma biologics therapy assessment following a population health management tool search.
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FeNO testing – Additional Covid-19 considerations
Always adhere to local and national Covid-19 guidance to maintain a safe environment for both primary care staff and public.
The following steps may be considered to maintain this safety:
• all are risk assessed and complete a pre-assessment Covid-19 screening questionnaire (see example below), prior to attending appointment including recording vaccination status and ensuring none display any signs nor symptoms of Covid-19 on the day of the scheduled test
• all patients are required to attend alone and wear a mask during appointment. They should remove mask only when instructed and cough into this mask if needed.
• where available and in-line with practice IPC guidelines, patients should be encouraged to undertake a Covid-19 Lateral Flow Test on the day of their appointment, due to the risk of coughing during the procedure.
• those with Long Covid-19 and on-going respiratory symptoms should be investigated and referred as per local Long-Covid care pathway by their primary care clinician.

Example pre-appointment Covid-19 screening questions

<table>
<thead>
<tr>
<th>Pre-appointment Covid-19 screening Questions</th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td>1. Have you tested positive for COVID-19 in the past 7 days?</td>
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<td>2. Are you a waiting a COVID-19 test result? For example, following travel abroad</td>
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<tr>
<td>3. Do you live with someone who has either tested positive for COVID-19 or had symptoms in the last 14 days?</td>
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<td>4. Have you had a high temperature (Above 37.8 °c)?</td>
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<td>5. Do you have a new continuous cough?</td>
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<td>6. Do you have a loss of smell or taste?</td>
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<tr>
<td>7. Have you been notified by NHS Test &amp; Trace in the last 14 days that you are a contact of a person (with whom you do not live) who has tested positive with COVID-19?</td>
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Answering Yes to any of the above questions should delay the FeNO test but should not delay essential care or management.

FeNO testing - pre-test preparation
Where possible an information leaflet should be provided ahead of the FeNO appointment, such as the example within the Wessex AHSN FeNO resources (see additional resources section). Also consider having information for the public accessible via the Primary Care Networks (PCN) and Primary Care practices' websites.
Ahead of a FeNO test the individual must be instructed to:
• Avoid eating, drinking (hot drinks, caffeine and alcohol) and smoking for at least 1 hour prior to their appointment
• Avoid any significant exertion or exercise for at least 1 hour prior to their appointment
• Avoid nitrate rich foods such as celery, leek, beetroot, lettuce, spinach or other green leafy vegetables, for at least 3 hours prior to their appointment.
Interpreting a FeNO test result
Interpretation of all FeNO tests should be undertaken by clinicians who are trained and competent in diagnosing asthma as well as have appropriate understanding of the value of FeNO in making a diagnosis (usually competence based).

When confirming an asthma diagnosis, FeNO test results should be considered in conjunction with a detailed clinical history, examination and additional tests assessing airways reversibility or diurnal variation.

The following algorithm (NICE Asthma: diagnosis, monitoring and chronic asthma management (2017)) can be used to guide the interpretation of test results from spirometry, FeNO and a completed peak flow diary. Alternative algorithms are available such as, for those under 17 years of age (see additional resources section).

In any settings where rapid access to FeNO and spirometry is not always available it is acceptable for clinicians to choose to use the BTS / SIGN British Asthma Guideline 2019 (see additional resources section).

Additional considerations when interpreting a FeNO test result
There are several confounding factors requiring additional caution when interpreting FeNO results. The following additional factors could be influencing the FeNO test result so should also be considered and excluded prior to advising alternative care.

The following factors that may lower FeNO levels and therefore results should be interpreted with caution before changing asthma management or excluding an asthma diagnosis:

- Inhaled and oral corticosteroid treatments
- Recent hot drink, caffeine and alcohol consumption
- Cigarette smoking
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The following factors that may raise FeNO levels and therefore results should be interpreted with caution before changing asthma management:

- sino-nasal disease such as allergic rhinitis
- a diet high in nitrate-rich foods such as leafy green vegetables
- an active respiratory tract infection

There are many other associations that have been made with a raised FeNO result that are non-respiratory, most of which would have symptoms of other problems. In a population study of FeNO in people without known asthma less than 1/3 with raised FeNO levels had any evidence of respiratory disease (after further testing, reversibility spirometry, challenge testing, bronchoscopy, sputum eosinophil analysis, bronchoalveolar lavage and imaging). Therefore, FeNO is not suitable as a general screening tool for the population and should only be undertaken when the result is likely to influence management.

Other considerations when presented with high or low FeNO results

- **Low FeNO level**:
  - <25ppb (<20ppb in children)
  - Consider differential diagnosis: Non-allergic asthma (non-ICS responsive, rhinosinusitis, bronchiectasis, cystic fibrosis, vocal cord dysfunction, breathing pattern disorder, GORD, cardiac disease

- **High FeNO level**:
  - >40ppb (>35ppb in children) or 40% increase from previous stable test result
  - Suggests ongoing inflammation, so ICS reduction may result in relapse. Check inhaler technique and compliance

- **Confirmed Asthma Diagnosis**
  - **Symptomatic**
    - Low FENO level <25ppb (<20ppb in children)
    - Consider differential diagnosis: Non-allergic asthma (non-ICS responsive, rhinosinusitis, bronchiectasis, cystic fibrosis, vocal cord dysfunction, breathing pattern disorder, GORD, cardiac disease
  - **Asymptomatic**
    - High FeNO level >40ppb (>35ppb in children) or 40% increase from previous stable test result
    - Suggests well-controlled inflammation (FeNO levels are reduced by ICS treatment). Could consider ICS reduction and re-check FeNO in 4 weeks. NOTE: 25-40ppb is also adequate ICS dosing in asthmatic unless 40% rise from previous test.

  - **At risk of exacerbation**.
    - Consider persistent allergen exposure, inadequate ICS dosage or poor inhaler technique or poor compliance

  - **Symptomatic**
    - Suggests ongoing inflammation, so ICS reduction may result in relapse. Check inhaler technique and compliance

  - **Asymptomatic**
    - Suggests well-controlled inflammation (FeNO levels are reduced by ICS treatment). Could consider ICS reduction and re-check FeNO in 4 weeks. NOTE: 25-40ppb is also adequate ICS dosing in asthmatic unless 40% rise from previous test.
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Unconfirmed diagnosis in symptomatic individual

**Low FeNO level**
- \(<25\text{ppb}\) (\(<20\text{ppb}\) in children)
- Suggests NO significant allergic eosinophilic airway inflammation (but alone does not rule out asthma)
- **ACTION:** Unlikely to benefit from ICS

**High FeNO level**
- \(>40\text{ppb}\) (\(>35\text{ppb}\) in children) or 40% increase from previous stable test result
- Suggests significant allergic eosinophilic airway inflammation
- **ACTION:** Likely to benefit from ICS

Consider differential diagnosis:
- non-allergic asthma, rhinosinusitis, bronchiectasis, Cystic Fibrosis, post viral bronchospasm, vocal cord dysfunction breathing pattern disorder, GORD, cardiac disease, pulmonary Hypertension, Pulmonary Embolism

Suggests significant allergic eosinophilic airway inflammation

**ACTION:** Likely to benefit from ICS

Consider differential diagnosis:
- allergic asthma, atopic asthma, allergic bronchitis, COPD with inflammatory phenotype

Recording a FeNO test result

It is important to record all FeNO test results in the primary care patient record system i.e. SystmOne, EMIS, preferably using the available ARDENs template. Where this template is not available then standard coding is acceptable. In other health care settings the test results should also recorded, ideally in a coded retrievable format. Accurate recording of test results ensures that all results are chronologically captured, contribute to an accurate patient care record and are retrievable for audit.

**Using ARDENs:** FeNO template - Diagnosis - Result – Respired Nitric Oxide concentration

**Using standard coding:** Measurement of expired Nitric Oxide; Y1fa5 [snomed 444642008]

Maintenance & cleaning of FeNO device

- All equipment should be part of the practices annual servicing schedule.
- FeNO devices will need either annual calibration or annual sensor replacement depending on the manufacturer/brand, therefore practices must follow the relevant manufacturers guidance.
- All sensors, filters and other components within the device should be replaced according to the manufacturer’s guidance, so as not to nullify the results gleaned from the testing.
- Where appropriate check consumables such as mouthpieces and filters are “in-date”
- External surfaces of devices should be cleaned with anti-microbial wipes that are **non-alcohol** based.
- Do not allow battery to fully discharge.
- Avoid exposing the FeNO device to extremes of temperature i.e. do not leave in direct sunlight on windowsill, do not leave in car overnight.
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Additional Resources


NICE (2017) asthma, diagnosis, monitoring and chronic disease management. Overview | Asthma: diagnosis, monitoring and chronic asthma management | Guidance | NICE


Circassia NIOX user manual, videos and other resources: Educational Videos – NIOX VERO® - United Kingdom

Bedfont NObreath user manual and other resources: The NObreath FeNO Monitor by Bedfont Scientific Ltd.


Wessex AHSN resources on the use of FeNO. Wessex AHSN Resources

Wessex AHSN patient communications and information leaflet. Asthma-FeNO_information leaflet

E-learning for health – free on-line FeNO modules: FeNO in Asthma - elearning for healthcare (e-lfh.org.uk)
Appendix I example of competency template for undertaking FeNO testing

All staff must be trained in how to use their specific brand of machine AND able to evidence their completing FeNO training such as the online learning module (E-learning for health) and the associated assessments before deemed competent to perform quality assured diagnostic FeNO.

Below are some example competency elements you may wish to include in an observed FeNO competency assessment use for delivery of the test. A competency assessment should be carried out by a clinician experience in FeNO testing. A minimum of 5 observed FeNO test is recommended to obtain competency.

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<thead>
<tr>
<th>Name (clinician)</th>
<th>Observed test</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>FeNO competency assessment</strong></td>
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<td>Observed correct preparation of FeNO device and all equipment required for safe practice.</td>
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<td>Confirms with patient the absence of contradictions to performing a FeNO test</td>
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<td>Provides clear explanation to patient of required technique for FeNO test</td>
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<td>Identify factors that may artificially increase or decrease FeNO test results</td>
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<td>Able to demonstrate how to add patient profile for specific FeNO device</td>
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<td>Observed ability to support patient to perform a valid FeNO test</td>
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<td>Discuss how FeNO testing can support in the diagnosis of asthma including the interpretation of results</td>
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<td>Discuss Infection Prevention &amp; Control measures including clinic &amp; device cleaning procedures</td>
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<th>Patient ID</th>
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<th>Comments</th>
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