**Technology:** Nitric oxide measurement system (NIOX®) for monitoring response to asthma treatment.

**Manufacturer:** Aerocrine AB, Stockholm, Sweden

**Purpose:** NIOX is a device that measures the concentration of nitric oxide in exhaled breath (eNO) as a marker of airway inflammation. It is marketed for use in doctors’ offices to monitor patients who have asthma and to assess their response to treatment. It is intended to complement, rather than replace, other clinical tests for asthma.

**Current Regulatory Status:** NIOX received a Medical Device Licence from Health Canada in 2004 and US Food and Drug Administration (FDA) marketing approval in 2003.1,2

**Description:** The NIOX system uses a chemiluminescence gas analyzer that can measure low concentrations of NO. The patient exhales through a mouthpiece that is connected to the analyzer. A flow control system maintains exhalation at 50 mL per second, regardless of the patient’s skill. A visual display guides the patient in maintaining an appropriate pressure range while exhaling.

**Cost:** A NIOX system is sold as a Start Package that includes computer, software, monitor, keyboard, calibration gas, installation and training. The US price is US$43,000. Operational costs include US$94 every six months to replace the NO scrubber (the filter that provides the instrument and the patient with NO-free air) and US$1,400 every 12 months for calibration gas. The NIOX system should be serviced every 18 months (US$3,000). There is a per test cost of US$4 for each disposable mouth piece filter (Jonas Stahlbage, Aerocrine Inc., Chicago: personal communication 2004 Apr 7).

**Evidence:** The FDA approval of the NIOX system was based on results from clinical studies involving 65 patients (adults and children aged four years and older) with confirmed diagnoses of asthma.2 The patients were tested using the NIOX system before they began drug treatment and two weeks later. The studies were conducted at nine medical centres in the US. The results showed that most patients had a 30% to 70% decrease of NO levels after two weeks of treatment with inhaled steroids. Exhaled NO levels above 30 parts per billion (ppb) correlated with moderate to severe asthma.2

The literature on the measurement of eNO is extensive. Several groups have reported the correlation of eNO levels with treatment for asthma. Details of some recent studies are summarized in Table 1.
## Emerging Technology List

### Nitric Oxide Measurement System (NIOX®) for Monitoring Response to Asthma Treatment

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) is a non-profit organization funded by the federal, provincial and territorial governments. (www.ccohta.ca)

<table>
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<tr>
<th>Study, Subjects</th>
<th>Results</th>
<th>Authors’ Comments and Conclusions</th>
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| Kharitonov *et al.*, 2003<sup>3</sup>  
Adults and children, 29 with mild asthma, 30 healthy individuals | Mean eNO values SS higher in those with asthma than in healthy individuals (adults 48.8 ppb versus 17.8 ppb, p<0.01; children 24.9 ppb versus 15.6 ppb, p<0.096). | Using NIOX was simple, measurements were reproducible and without diurnal or day to day variation |
| Meyts *et al.*, 2003<sup>4</sup>  
78 children aged between 5 and 16 | eNO levels in those with insufficient asthma control, as judged by clinical and spirometry findings, SS higher than for those with good or acceptable control | Substantial overlap in concentrations between patient groups, making interpretation of eNO values for individual patients difficult |
| Covar *et al.*, 2003<sup>5</sup>  
30 children treated with budesonide and 52 individuals given a placebo, followed by discontinuation of treatment | eNO levels SS lower in steroid-treated group, but no difference between groups after 2 to 4 month washout following discontinuation of treatment | Suggest that eNO may serve useful role in measuring response to medication change and assessing patients’ compliance |
| Beck-Ripp *et al.*, 2002<sup>6</sup>  
34 children with persistent asthma; four week run-in and run-out periods (with or without treatment) followed by randomization to treated and non-treated groups | • eNO levels reduced to normal values during run-in period, then increased during washout; in 15 children then randomized to steroid treatment, eNO decreased, whereas it remained unchanged in 16 untreated patients  
• Forced expiratory volume in one second and forced vital capacity at rest and after exercise SS improved after run-in period, but showed no difference after randomization; strong correlation of eNO with treatment compliance during run-in period (results for 17 individuals are reported) | eNO differentiated between children treated with or without steroids, whereas conventional lung-function variables could not; eNO may be valuable tool for monitoring medication compliance but less useful in detecting physiologically relevant changes in lung function |
| Jones *et al.*, 2001<sup>7</sup>  
78 patients with mild to moderate asthma had inhaled steroid therapy withdrawn until loss of control (LOC) occurred or for maximum of 6 weeks | 77.9% developed LOC; eNO measurements had positive predictive values of 80% to 90% for predicting and diagnosing LOC; these values similar to those obtained using measurements of sputum eosinophils and airway hyper-responsiveness to saline | eNO measurements as useful as induced sputum analysis and airway hyperresponsiveness in assessing airway inflammation; advantage is that they are easier to perform |
The gold-standard technique for monitoring airway inflammation is bronchoscopy with lavage and biopsy, but induced sputum analysis is also used. The cost and the invasiveness of these techniques, however, restrict their routine use in clinical practice. As a result, pulmonary function tests, such as spirometry, are commonly used to assess asthma, though they do not reflect the extent of airway inflammation. There is evidence that spirometry provides only a delayed indication of changes in the use of corticosteroids.\(^8\)

NIOX is another option for the clinical assessment of patients’ compliance and response to medication. It has advantages over some other methods in that it is linked to the extent of airway inflammation. The device can be used by children over the age of four.

NIOX is a high-cost device that might be most commonly used in clinics or practices with large numbers of patients with asthma. The measurement of exhaled NO is also being investigated for applications in chronic obstructive pulmonary disease, cystic fibrosis and chronic cough.\(^9\)

No information was found on the extent to which the use of this device improves patients’ compliance with medication use or ensures appropriate prescribing. Comparative studies to obtain such measures of efficacy would be desirable.

References:


This summary was prepared by David Hailey, PhD, CCOHTA.

This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

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