Nitric oxide is a cellular signalling molecule with wide-ranging cardiorespiratory effects including pulmonary vasodilation, bronchodilation, alveolarisation, angiogenesis and inhibition of inflammation. Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator commonly used to treat neonates with respiratory failure. Although it received regulatory approval in Europe in 2001 for use in hypoxaemic respiratory failure associated with pulmonary hypertension in neonates >34 weeks’ gestation, it is often used outside this licensed indication (off-label) in preterm neonates. Rates of iNO usage in newborn infants vary considerably between centres.

The European Inhaled Nitric Oxide Registry is an international collaboration originally established as a pilot project in 2006 and formally launched in September 2009. Anonymised data are submitted online using a web-based data form and held securely in a central data repository managed by MedSciNet, an internet database provider that also runs other similar projects (eg the Swedish National Perinatal Quality Registry) and a variety of high profile international randomised controlled trials. The project is currently funded through a combination of charitable sources and commercial

Keywords
inhaled nitric oxide; newborn infant; persistent pulmonary hypertension of the newborn; hypoxaemic respiratory failure; bronchopulmonary dysplasia

Key points
1. Data on the use of iNO therapy can be submitted online to the European Inhaled Nitric Oxide Registry.
2. This information adds to the body of observational research on iNO therapy and will allow reporting on issues relating to the safety and efficacy of iNO therapy in infants.
3. Data from the registry will inform the design of future clinical research trials of iNO therapy and decisions about regulatory approval for new indications.
4. The registry supports education and training around the use of iNO and promotes greater collaboration between units using iNO.
sponsors; there is no charge to individual collaborating units.

The aim of the registry is to collect and report information regarding episodes of iNO treatment in children, including data on patient demographics, indications for treatment, delivery and administration of iNO, thresholds for treatment, concomitant treatments, potential adverse effects of therapy and clinical outcomes. Specifically, these data will allow:
- monitoring of the range of indications for which iNO is used in routine clinical practice, including quantifying unlicensed use
- identification of adverse events associated with iNO therapy (a post-marketing surveillance role)
- promotion of consistent, high standard, clinical management among clinicians using iNO through newsletters and educational events
- generation of research hypotheses that can be tested formally in the context of properly designed clinical trials
- support of future clinical trials of iNO therapy by, for example, informing discussions about sample size calculation
- monitoring trends of iNO usage in relation to other cardiorespiratory therapies such as extracorporeal membrane oxygenation
- support for regulatory bodies in making decisions about future drug licensing.

A recent review paper underlined the role and importance of multicentre registries in addressing issues relating to the safety and efficacy of iNO in preterm infants with persistent pulmonary hypertension of the newborn (PPHN) physiology. Individual units can access and use their own uploaded data to provide information for local audit and research purposes. The opportunity to use data held in the registry for ethically approved research is also available.

To date, information has been collected from over 1,553 children treated with iNO from 44 neonatal and paediatric intensive care units in 13 countries (FIGURE 2). Twenty-six neonatal intensive care units in the UK have registered.

Approximately half of all treatment episodes in the registry relate to off-label iNO therapy in preterm infants of <34 weeks’ gestation. TABLE 1 summarises the underlying diagnoses in neonates receiving iNO therapy.

Data from the registry have been presented at various international scientific meetings and published as original papers. The registry has demonstrated that this information can be collected and reported successfully, adding novel material to the existing body of observational research on iNO therapy.

### References


For more information about joining the iNO Registry please contact:

Julie Wray julie.wray@lwh.nhs.uk or Nim Subhedar nim.subhedar@lwh.nhs.uk