

Online supplement

## Supplementary Methods

### *Approach to FeNO suppression*

- Identify appropriate patient- referred to Difficult Asthma Clinic, uncontrolled despite Step 4 or already requiring Step 5 treatment as per GINA guidelines.
- Consider FeNO suppression if  $\text{FeNO} \geq 45 \text{ppb}$ .
- Review of subject's inhaler technique with currently prescribed device undertaken. Subject advised to continue with this treatment as prescribed for the duration of the week's monitoring.
- Demonstration of measurement of FeNO using Niox VERO machine
- Subject asked to perform FeNO each morning and note the reading on the provided table.
- Preparation of INCA™ device on Flixotide '500' Diskus device
- Subject shown how to use Diskus device, and advised to take 2 inhalations in the morning for 7 consecutive days after they have measured their FeNO, and tick on provided table when taken.
- Appointment made for 7 days later to collect data, and upload INCA™ device data to Vitalograph IC Data Compression Utility server (with additional input of FeNO readings, eosinophils and ACQ result) and an overall adherence measure obtained.

### *Acoustic Monitoring Technology*

The INCA™ device is used with the Diskus device. When the device is opened the microphone is activated and recording begins, but automatically stops after 90 seconds if the device is left open. The recording stops when the device is closed.

Sound files are subsequently analysed by the INCA™ Analysis software and assess if the inhalation has been taken appropriately (figure 1); "technique errors" could be reviewed and manually over-read by the clinical team. Feedback was generated into graphical form regarding technique and usage alongside FeNO (figure 2).

### *Positive FeNO suppression test*

As previously discussed [8], a positive FeNO suppression test was defined as  $\text{Lg10}\Delta\text{FeNO}$  greater than or equal to 0.24 where  $\text{Lg10}\Delta\text{FeNO}$  was calculated as  $\{\text{mean}(\text{Lg10 FeNO Day 0}, \text{Lg10 FeNO Day 1})\} - \{\text{mean}(\text{Lg10 FeNO Day 4}, \text{Lg10 FeNO Day 5})\}$ . A fall in FeNO of 43% or greater between the Day 0/ Day 1 and Day 4/ Day 5 mean values indicates a positive test.

Figure 1. Example of sound file and semi-automated analysis

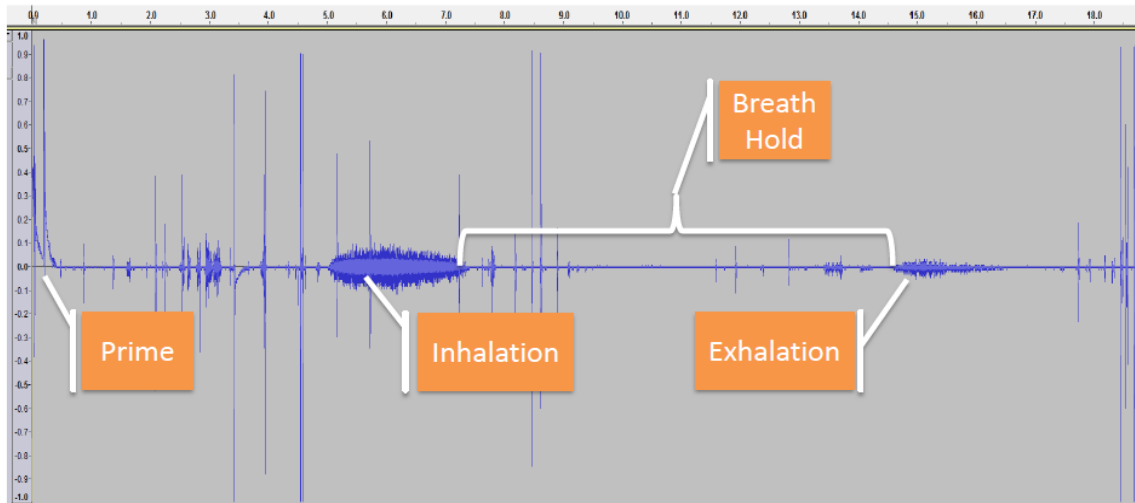


Figure 2. Example data from the Vitalograph server. Figure 2a depicts percentage change in FeNO from baseline on the y1-axis, and doses taken per day along the y2-axis. Figure 2b depicts technique analysis.

Figure 2a

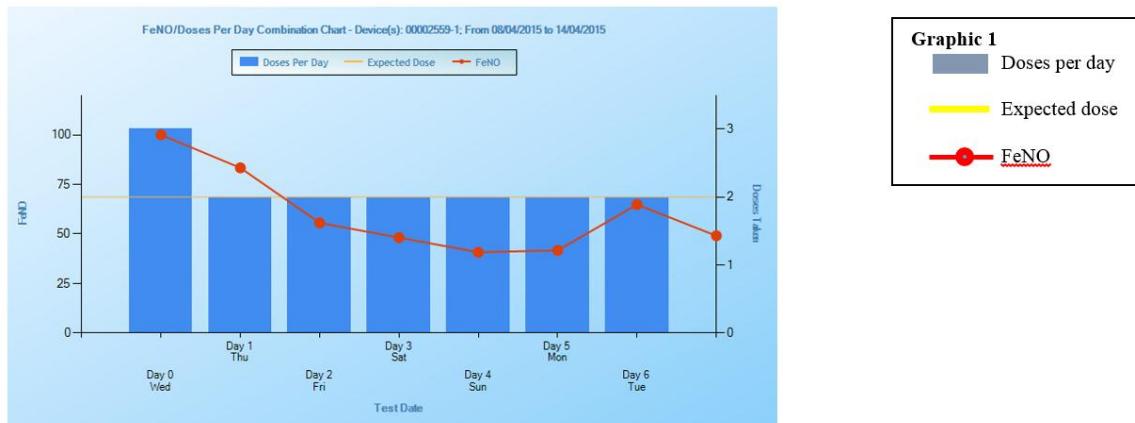


Figure 2b

