Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with Boehringer Ingelheim’s Policy on Transparency and Publication of Clinical Study Data.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country.

Additional information on this study and the drug concerned may be provided upon request based on Boehringer Ingelheim’s Policy on Transparency and Publication of Clinical Study Data.

The synopsis is supplied for informational purposes only in the interests of scientific disclosure. It must not be used for any commercial purposes and must not be distributed, published, modified, reused, posted in any way, or used for any other purpose without the express written permission of Boehringer Ingelheim.
### Name of company:
Boehringer Ingelheim

### Name of finished product:
Berodual® Respimat® and Berodual® Metered Dose Inhaler

### Name of active ingredient:
Ipratropium bromide and fenoterol hydrobromide

### Ref to Documentation:

<table>
<thead>
<tr>
<th>Volume</th>
<th>Page</th>
<th>Addendum No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U05-1746</td>
<td></td>
</tr>
</tbody>
</table>

### Report date:
20 JUN 2005

### Study period (years):
17 APR 03 – 22 DEC 04

### Title of study:
A randomised open label, six way, cross-over scintigraphic evaluation of the effect of inspiratory flow rate on lung and oropharyngeal deposition with the Respimat® inhaler vs a Metered Dose Inhaler (HFA-MDI) using Berodual® in patients with Chronic Obstructive Pulmonary Disease (COPD)

### Investigator:

### Study center:

### Publication (reference):
N/A

### Clinical phase:
IIIb/IV

### Objectives:
To compare the lung and oropharyngeal deposition of Berodual® (fenoterol hydrobromide 50µg + ipratropium bromide 20µg /1x puff) delivered via the Respimat® inhaler and the same dose of Berodual® delivered via a hydrofluoroalkane - metered dose inhaler (2 x puffs ) in COPD patients at different inspiratory flow rates.

### Methodology:
Gamma scintigraphy

### No. of subjects:
- planned: entered: 12
- actual: entered: 3
  - Treatment A: Berodual® in Respimat® and metered dose inhaler
    - entered: 3  treated: 3  analysed: 3
  - Treatment B: Berodual®
    - entered: 3  treated: 3  analysed: 3
- enrolled: 3

### Diagnosis and main criteria for inclusion:
Males and non-pregnant females with COPD

### Test product:
- Treatment A
  - dose: Ipratropium bromide 20µg and fenoterol hydrobromide 50µg
  - mode of admin.: Inhalation via Respimat®
  - batch no.: N/A
# Boehringer Ingelheim Limited
**BI Trial No.: 215.1361**

## Name of company:
Boehringer Ingelheim

## Name of finished product:
Berodual® Respimat® and Berodual® Metered Dose Inhaler

## Name of active ingredient:
Ipratropium bromide and fenoterol hydrobromide

## Ref. to Documentation:

<table>
<thead>
<tr>
<th>Volume:</th>
<th>Page:</th>
<th>Addendum No.:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Report date:
20 JUN 2005

## Study period (dates):
17 APR 03 – 22 DEC 04

## Duration of treatment:
One administration of Berodual® (fenoterol hydrobromide 50µg + ipratropium bromide 20µg /1x puff) delivered via the Respimat® inhaler and the same dose of Berodual® delivered via an hydrofluoralkane - metered dose inhaler (2 x puffs ) in COPD patients at different inspiratory flow rates.

## Reference therapy:
**Treatment B**
- **dose:** Ipratropium bromide 20µg and feneterol hydrobromide 50µg+
- **mode of admin.:** Inhalation via Respimat® and metered dose inhaler
- **batch no.:** N/A

## Criteria for evaluation:

<table>
<thead>
<tr>
<th>Efficacy:</th>
<th>Safety:</th>
<th>Statistical methods:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deposition of aerosol assessed via gamma scintigraphy</td>
<td>Physical examination, ECG, Adverse Events</td>
<td>Sign test</td>
</tr>
</tbody>
</table>

## SUMMARY – CONCLUSIONS:
**Efficacy results:**
N/A

**Safety results:**
There were no safety issues.

**Conclusions:**
Due to the investigator’s difficulty in recruiting eligible patients, the 215.1361 study was terminated early with only 3 out of the 12 planned patients treated. The limited 215.1361 study results indicate that different inspiratory flows from a metered dose inhaler do not appear to affect the amount of drug reaching patients’ lungs. However, using the Respimat® inhaler, the lower the inspiratory flow, the greater the amount of drug delivered to the lungs.

At the lowest inspiratory flow investigated in the 215.1361 study (15 l/min), approximately twice as much drug reached the lungs using the Respimat® inhaler compared to a metered dose inhaler.