

## **APPENDIX V**

### **CLINICAL TRIAL INFORMATION LEAFLET**

#### **Clinical Trial to Assess the Tolerability of an Inhaled Antibiotic (Protocol No.COLO/DPI/98/02)**

Colistin is an antibiotic medicine that has been marketed in the UK for over 37 years for the treatment of certain chest infections in cystic fibrosis. Patients can either inhale colistin using a device called a nebuliser, or be given colistin by an injection.

The company that sells colistin has developed a new formulation for inhaling the drug. The new formulation is a powder contained in capsules, which is breathed in through a pocket-sized, hand held device. Colistin powder is made of the same ingredients as standard colistin, but has been made into a much finer powder.

Before colistin powder can be given to patients with cystic fibrosis who have chest infections, it is necessary to show that the drug is acceptable to volunteers who have cystic fibrosis. Therefore, we would like to invite you to take part in a research project in which we are going to look at how you tolerate colistin powder when it is breathed in. You will not gain any clinical benefit from participating in this trial.

The study will consist of 5 separate visits to the Adult CF Centre at Southampton General Hospital over a period of up to 6 weeks. Each visit will involve you spending a large part of the day in the unit. At the first visit you will receive a thorough medical and you will be asked questions about your health. We will also require permission to contact your GP to inform them of your participation. At each of your subsequent visits you will receive a single dose of inhaled colistin and the adult CF staff will measure any changes in your breathing using a special machine. It may also be necessary for certain officials from the sponsoring drug company or government regulatory authorities to read your medical notes. These people understand the need for confidentiality.

To evaluate the effect of this drug, it will be necessary to attend for a full day on the four main study days. You will be compensated for your time and expenses.

#### **Taking part in this study is entirely voluntary:**

Please take as much time as is necessary to decide whether or not to take part in this study. If you decide to take part you can change your mind at any time and withdraw without giving any reason. If you decide not to take part in the study from the beginning or if you decide to withdraw at any time during the study, it will not affect the medical care that you receive either now or in the future. The doctor is also able to withdraw you from the trial at any point if they feel there is good reason (e.g. if it is in your interests to do so).

#### **What will happen to you?**

Before you come to hospital for each of your visits, it is important that you observe the following restrictions so that the drug can be adequately assessed:

- Do not eat any chocolate (including drinks like cocoa), or drink any tea, coffee, cola or alcohol from midnight of the previous day to your visit.
- Do not use your bronchodilator from midnight of the previous day to your visit (If you do need to use your inhaler during this period, please contact Clare Forsythe prior to attending the department or inform Clare Forsythe or Jane Wilkinson when you arrive).

During each of the next 4 visits, you will be given one of the following 4 doses:

- a standard dose of colistin that you will breathe in through a nebuliser device (this takes about 30 minutes).
- a single dose of inhaled lactose using a pocket sized hand-held device.



- a single dose of salbutamol (this clears your chest) and then a single dose of inhaled colistin powder using a pocket sized hand-held device.
- a single dose of inhaled colistin powder only using a pocket sized hand-held device.

By the end of the study you will have been given each of the four doses, one per day. The doses will however be given in a random order. The order in which you receive the doses will be decided by a computer, by chance.

Before and after each dose, the staff will monitor your breathing using a special machine called a spirometer.

During the study the CF nurse will need to take a total of 8 separate blood samples from you (approximately equal to 5 tablespoons). It will also be necessary to collect samples of urine from you during each visit. A drugs of abuse screen and pregnancy test (for women) will be conducted on one of these urine samples.

#### **Are there any hazards?**

Previous studies of patients with chest infections and healthy volunteers have shown that colistin is safe when inhaled. Major side effects have not been reported but there is the possibility of some side effects, such as tightness in the chest, dizziness, pins and needles or numbness. In addition it is likely that when you inhale colistin powder it will make you cough.

Most people do not have any problems when taking salbutamol. However some may occasionally feel a bit shaky, get muscle cramps or have a headache. A few may feel their heart beat faster or experience mouth or throat irritation.

If any symptoms such as these do occur, they should not last very long. Jane Wilkinson, who will be monitoring you, will wish to know if you are experiencing any side effects.

For women:-

It is important that you do not become pregnant during this study. You should not participate in this study if you are pregnant or breast-feeding.

#### **Why is this research important?**

Inhaled colistin is an important part of treatment for certain chest infections. Treatment with inhaled colistin always used to be given in hospital but now is more commonly given at home. Traditional treatment demands more time and preparation than colistin powder and requires expensive devices. It will be a definite advantage for patients if this therapy can be simplified by giving colistin as a powder.

#### **Who can I contact for more information?**

If you would like further information or if you have any further questions about the study please contact



**APPENDIX VI**  
**CONSENT FORM**

**A RANDOMISED, OPENLABEL STUDY TO COMPARE TOLERANCE AND BRONCHIAL  
RESPONSE TO NEBULISED COLISTIN AND COLISTIN DRY POWDER INHALATION IN  
VOLUNTEERS WITH CYSTIC FIBROSIS.**  
**PROTOCOL NO: COLO/DPI/98/02 (LREC REF. No)**

Subject Number

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Subject Initials

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**Parts A, B & C MUST be completed before the subject is entered into the study.**

**PART A**

	Please tick	
	YES	NO
1. Have you read the clinical trial information leaflet provided?	<input type="checkbox"/>	<input type="checkbox"/>
2. Has the nature and purpose of the study been explained to you?	<input type="checkbox"/>	<input type="checkbox"/>
3. Have you had the opportunity to ask questions and discuss the study?	<input type="checkbox"/>	<input type="checkbox"/>
4. Have you received satisfactory answers to your questions?	<input type="checkbox"/>	<input type="checkbox"/>
5. Have you received enough information about the study?	<input type="checkbox"/>	<input type="checkbox"/>
6. Have you had adequate time in which to decide whether to participate? in the study?	<input type="checkbox"/>	<input type="checkbox"/>
7. Who has spoken to you about the study? Prof./Dr/Mr./Mrs./Ms _____		

**PART B**

	Please tick	
	YES	NO
1. Do you understand that participation in the study is voluntary and that you are free to withdraw at any time (you do not have to give a reason for withdrawing and it will not affect your future medical care)?	<input type="checkbox"/>	<input type="checkbox"/>
2. We know that you would want your medical records to be kept confidential. However, during the study it will be necessary for certain officials (i.e. the sponsor, Government Regulatory Authorities or the Hospital Ethics Committee) to look at your medical notes (these people understand the need for confidentiality). In addition to this, do you authorise Medical Specialties to contact your GP to make known your participation in this study and to disclose details of your relevant medical and drug history, in confidence?	<input type="checkbox"/>	<input type="checkbox"/>
3. Do you understand that if you should suffer injury as a result of participating in this study the sponsor agrees to operate in good faith by the "Clinical Trial Compensation Guidelines" published in 1991 by the Association of the British Pharmaceutical Industry?	<input type="checkbox"/>	<input type="checkbox"/>

**PART C**

SUBJECT: I \_\_\_\_\_ hereby consent to take part in the above-titled  
(Subject's full name – in their own handwriting) study, the nature and purpose of which I understand.

Signed: \_\_\_\_\_ Date: \_\_\_\_\_  
(Subject's signature)

INVESTIGATOR: I hereby declare that I have discussed the above-titled study in accordance with GCP Guidelines.  
The subject has understood all the information he/she has been given and freely chooses to participate in this study.

Signed: \_\_\_\_\_ Date: \_\_\_\_\_  
(Investigator's Signature)



**APPENDIX VII**  
**LETTER OF NOTIFICATION TO GENERAL PRACTITIONER OF VOLUNTEER**  
**INFORMING OF INTENDED PARTICIPATION IN CLINICAL TRIAL - CYSTIC FIBROSIS**  
**VOLUNTEERS**

*[Headed paper from centre]*

Protocol No. COLO/DPI/98/02

Date

LREC Ref.:

<i>Name of GP</i>
<i>Address of GP</i>

Dear (*Name of GP*)

**Re: (*Name of Volunteer - Date of Birth of Volunteer*)**

Your patient, (*name of volunteer*), intends to participate in a non-therapeutic clinical trial to assess the safety and tolerability of an inhaled antibiotic (colistin) in volunteers with cystic fibrosis.

Each volunteer will attend the Adult CF Centre during the daytime on 5 separate occasions. At the first visit, the volunteer will undergo a full medical screen (including biochemical and haematological tests), a review of their personal medical history and a physical examination.

During the next 4 visits, each volunteer will receive a single dose of inhaled medicine both with and without bronchodilating pre-medication. This product has already been found to be safe in healthy volunteers. The antibiotic being evaluated is specifically intended for use in patients with cystic fibrosis.

Volunteers for this phase of the project are expected to be:

- ☐ *Free from any known sensitivity to colistin sulphomethate or salbutamol*
- ☐ *Free from any current CF related exacerbation*
- ☐ *Free from a history of alcoholism and drug abuse*

If you should have any concerns regarding this volunteer's participation, please do not hesitate to contact (*name of Adult CF Centre Contact*) Respiratory Medicine, [REDACTED] *telephone number of contact*).

Yours Sincerely,

(Name of Adult CF Centre Contact)  
(Department Title of Contact)

