

APPENDIX V**CLINICAL TRIAL INFORMATION LEAFLET****Clinical Trial to Assess the Tolerability of an Inhaled Antibiotic (Protocol No.COLO/DPI/98/01)**

Colistin is an antibiotic medicine that has been marketed in the U.K. for over 37 years for the treatment of certain chest infections. Patients can either inhale colistin using a device called a nebulizer, or be given colistin by an injection. In both cases colistin is supplied in glass vials and has to be reconstituted with sterile water.

The company that sells colistin has developed a new formulation for inhaling the drug that may offer advantages over standard treatment. Instead of using expensive nebulizing equipment, 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 chest infections, it is necessary to show that the drug is acceptable to 12 *healthy volunteers/volunteers who have mild asthma/ volunteers who have cystic fibrosis (* **Delete as appropriate**). 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 4 separate visits to Southampton General Hospital over a period of up to 6 weeks. Each visit will involve you spending a large part of the day in our research 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 hospital staff will measure any changes in your chest using a special machine. It may also be necessary for certain officials to read your medical notes. These people understand the need for confidentiality.

If you agree to take part in this study, you must be prepared to attend each of the visits. During each visit you must also be prepared to stay in hospital during the daytime, because of the need to monitor you very carefully during this time. You will be compensated for your time and expenses.

Taking part in this study is entirely voluntary:

You are allowed as much time as is necessary to decide whether 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 standard of 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:

1. 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.
2. If you suffer from asthma or cystic fibrosis, 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, contact the study nurse prior to attending the department or inform the study nurse or doctor when you arrive).

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3. If you do not suffer from either asthma or cystic fibrosis, you must not take any medicines other than paracetamol or contraceptives during the 7 days previous to your visit.

During your next visit, you will receive a standard dose of colistin that you will breath in through a nebulizer device (this takes about 30 minutes). During the visit after this, you will receive a single dose of salbutamol (this clears your chest) and then a single dose of colistin powder using a pocket sized device. At the last visit, you will receive a single dose of colistin powder only.

Before and after each dose, the staff will monitor your chest using a special machine called a 'Box'. The Box is made from transparent plastic and you are required to sit on a seat inside it during the measurements.

During the study the Doctor will need to take a total of 8 separate blood samples from you. It will also be necessary to collect samples of urine from you during each visit. A drugs of abuse screen and pregnancy test (if applicable) will be conducted on one of these urine samples.

Are there any hazards?

Previous studies of patients with chest infections have shown that standard 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. If symptoms such as these do occur, they should not last very long. The doctor monitoring you will wish to know if you are experiencing any side effects.

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 Dr. _____ on tel. No. 01703 (_____) or Research Nurse Karen Sampson on tel. No. 01703 (_____).



APPENDIX VI
CONSENT FORM

**AN OPEN LABEL STUDY TO COMPARE TOLERANCE AND BRONCHIAL RESPONSE TO
NEBULIZED COLISTIN AND COLISTIN DRY POWDER INHALATION IN HEALTHY,
MILDLY ASTHMATIC AND CYSTIC FIBROSIS VOLUNTEERS.**
PROTOCOL NO: COLO/DPI/98/01

Subject Number

Subject Initials

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

<u>PART A</u>	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 _____		

<u>PART B</u>	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 University Medicine 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"/>

<u>PART C</u>
<p>SUBJECT: I _____ hereby consent to take part in the above-titled study, the nature and purpose of which I understand. (Subject's full name – in their own handwriting)</p> <p>Signed: _____ Date: _____ (Subject's signature)</p> <p>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.</p> <p>Signed: _____ Date: _____ (Investigator's Signature)</p>

