

## **APPENDIX B (NON-USA SITES ONLY) PATIENT INFORMATION SHEET**

**A randomised, multicentre, double-blind, double-dummy trial comparing CP-99,219 with amoxycillin and optional erythromycin for the treatment of community acquired pneumonia. 154-112-000**

Before you decide to take part in this study, it is important that you read this sheet which provides you with the information on the study you are being asked to participate in. Your doctor will in any event be discussing the content of this sheet with you, but when you have read it and you feel that you would like to discuss any particular point further please ask your doctor who will be happy to explain any statement made.

If, when you have read all the information, you decide you would like to take part in this study, please sign the sheet at the place indicated and return it to your doctor; a copy will be given to you.

You are being asked to take part in a research drug study. This study is being done to compare the effects of an experimental drug called CP-99,219 with standard therapy for the treatment of an infection like your pneumonia. As CP-99,219 is a research drug it is only available to you for the purpose of the study and will not be available afterwards. It is very important that you follow the requirements of the study.

Around 360 patients with various infections took CP-99,219 at doses that have ranged from 50 to 300 mg daily for up to 14 days. These studies are still on-going. So far there have been no serious side effect due to CP-99,219. Around about 8% of patients stopped taking their medication for untoward effects. This level was similar to that seen with the standard antibiotics (7.1%) they were being compared to. The main side effects seen in some people were drowsiness, nausea, sickness, mild short-lived light-headedness, headache, skin rash and itching. The other drugs that are being used in this study are standard antibiotics: amoxycillin and erythromycin. These also are associated with various side effects like upset stomach, rashes and various blood test abnormalities. As with any new drug, there is the possibility of complications and undesirable side effects which are unknown at this time and could possibly occur. You will be told of any new serious risk to which you will be exposed.

If you agree to join this study you will undergo a physical examination including a chest X-ray. A sample of your blood will be taken. You will need to provide a sample of urine and sputum. These tests are being done to check that you are suitable for the study. If you cannot produce an adequate specimen of sputum, the doctor may want to use other measures to obtain material for culture, which will be explained to you.

If you begin taking study medication you will be seen by your doctor on a further 3 occasions. Each time you will be examined by the study doctor. Further samples of sputum will be needed on the second and third visit. Blood samples will be needed at all 3 follow up visits. The chest X ray will be repeated on the third, and if still abnormal on the fourth visit. You will need to show your medicine to the doctor on the second and third visit. At all visits you must tell your doctor of any symptoms you have suffered during your illness.

It is very important that you take all the medication as instructed by the doctor. Neither you nor your doctor will know whether you will be taking CP-99,219 or the standard therapy. This information is however available in an emergency. You will be provided with a blister pack containing your medication. You must take the medicine as described on the blister pack. At the second visit between day 3 to 5 the doctor will decide how long you need to take the medicine for. The total period may be either 7 or 10 days. Whatever the length of therapy the medicine still needs to be taken at the same times each day. On the first day of treatment the doctor may decide that you require an additional drug. This will be provided in a separate container. If given this container you will need to take, as well as all the other pills, two pills from this container every six hours. The doctor will tell you how long this needs to be taken for.

It is important to know that if you do not wish to take part in this study there are alternative antibiotic therapies available to you. Further, if you do agree to enter this study you are free to withdraw at any time but you must tell your doctor of this decision. Such withdrawal will not affect your future treatment or your relationship with your doctor.

The study will last approximately 35 days. You will see the doctor on four occasions. These are before treatment, called day 1, between day 3 to 5, between day 9 to 15 and finally between day 28 to 35. It is important to keep these appointments. The doctor or the sponsor can remove you from the study without your consent based on their judgement to improve your medical care or because of your failure to follow the study requirements.

In case you need to be seen by another doctor it is important that he knows you are in a research study. You will therefore be given a card that says you are in a study and which has a telephone number for the doctor to contact if he requires to do so. You must carry this card at all times and return it at the end of the study to the study doctor. If you do see another doctor please let your study doctor know.

You should contact the doctor if you have any questions about the conduct of the study, your rights as a patient or if you have any questions concerning possible side effects.

The study is being done at other centres. In total we expect around 320 patients to join the study.

Women of childbearing potential can enter this study but must have a negative pregnancy test before treatment. They must also use adequate contraception, including barrier methods, both during and for 1 month after the end of the study. Nursing mothers and pregnant women must not be treated in this study. You are not allowed to donate blood during the study or for one month after its completion.

All clinical records relevant to this study may be reviewed by the sponsor or its designees but will be treated as confidential. Information from this study may be submitted to government agencies as support for drug approval, such agencies may wish to review individual case notes. The results of this research project may be presented at research meetings or in publications. However in all instances your identity will not be disclosed.

The sponsor of this study does not expect you to suffer any health problems by taking part in this trial. They do carry insurance to make sure that anyone whose health suffers as a result of being in the trial can be compensated. You do not have to prove that it was anyone's fault if the problem arose because of the trial.

**APPENDIX C (NON-USA SITES ONLY)****PATIENT CONSENT FORM (OR AGREEMENT TO PARTICIPATE)**

**A randomised, multicentre, double-blind, double-dummy trial comparing CP-99,219 with amoxycillin and optional erythromycin for the treatment of community acquired pneumonia. 154-112-000**

**Notes to Investigator**

It is the responsibility of the Investigator to ensure that the patient is fully informed of the nature of the study, the drugs to be administered and the investigations to be performed with their attendant risks and benefits, in language that is readily understandable by the patient and in such detail as is required for the patient to be able to make a properly informed decision.

It is preferable that such information is given to the patient in typed or printed form and that he is given adequate time to consider the issues before being required to make the decision whether or not to participate. As the level of detail required will vary from patient to patient, it is expected that any written explanation will require oral expansion to some extent. The Patient information sheet provided in Appendix B is considered to be the minimum written explanation required.

**PATIENT CONSENT FORM (OR AGREEMENT TO PARTICIPATE)  
(NON USA SITES ONLY)**

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**Patient's Name:** ..... 154 112 \_\_\_\_\_ .....

1. The above named patient agrees to take part in this clinical study.
2. The patient (and parent/guardian if appropriate) has been given a full explanation of the purpose of the study, of the procedures involved and of what (s)he will be expected to do. (S)he has been told by the supervising doctor about possible ill effects on his/her health and well-being which might result from his/her participation.
3. The patient (and parent/guardian if appropriate) has informed the supervising doctor of any medication/ drugs, of whatever nature, that (s)he has taken in the last 28 days, or is now taking, or planning to take, whether prescribed or not.
4. The patient (and parent/guardian if appropriate) agrees to cooperate fully with the supervising doctor, and to inform him/her immediately if (s)he suffers any unexpected or unusual symptoms.
5. The patient will not donate blood during the period of the study or for one month after the end of the study.
6. The patient (and parent/guardian if appropriate) understands that (s)he is free to withdraw from the study at any time.
7. It is agreed that the patient will not be referred to by name in any report concerning the study in question or disclosed to any other person. The patient shall not claim to be entitled to restrict in any way the use to which the results of the said study may be put. In particular, the patient agrees to disclosure of any report of those results to Regulatory authorities.
8. The patients (and parent/guardian if appropriate) understands that the information in their medical records is essential to evaluate the results of the study. The patient agrees to the release of this information on the understanding that it will be treated confidentially.

**Signature by the patient  
(and parent/guardian if appropriate)**

**Signature by the Supervising doctor**

**Signed:** .....

**Signed:** .....

**Name (please print):** .....

**Name:** .....

**Signed:** .....

**Date:** .....

**Name (please print):** .....

**Date:** .....

## APPENDIX D

### HEPATIC AND OTHER LABORATORY SAFETY

Moderate and marked liver function abnormalities will be defined as follows:

	AST/ALT (SGOT/SGPT)	Alkaline Phosphatase	Total bilirubin
Moderate	>1.5 x ULN	>1.2 x ULN	>1.5 x ULN
Marked	>3 x ULN	>1.5 x ULN	>2.0 x ULN

where ULN is defined as the upper limit of normal if the pretreatment baseline was normal, or the pretreatment baseline if it was abnormal.

Moderate abnormal liver function tests should be repeated within 3 to 7 days. If they are confirmed, they should be repeated at weekly intervals until they resolve.

Patients with marked liver function abnormalities must discontinue treatment immediately, and the Pfizer appointed monitor must be notified. The abnormal tests should be repeated within 48 hours, and then at 3 to 7 day intervals until they resolve. In consultation with the Pfizer appointed monitor, additional evaluation of the patient with marked abnormalities that persist after study drug treatment is discontinued should be arranged. The additional evaluation may include GI consultation and additional laboratory tests (e.g. HBV, HAV, or CMV serology; CPK; reticulocyte count).

Rechallenge may be considered only after the responsible Ethics Committee and the Pfizer project clinician agree, and informed consent has been obtained.

In addition, any of the following marked laboratory abnormalities will lead to automatic additional central laboratory testing on stored samples. This data will be reviewed by a Pfizer clinician, and in consultation with the investigator, additional laboratory evaluation may be performed.

Bilirubin increase from baseline	$\geq 1.0$ mg/dL or $\geq 17$ $\mu$ mol/L
Creatine increase from baseline	$\geq 0.8$ mg/dL or $\geq 73$ $\mu$ mol/L
Hemoglobin decrease from baseline	$\geq 2$ g/dL or $\leq 1.24$ mmol/L