The early use of Antibiotics in at Risk CHildren with InfluEnza
Nuffield Department of Primary Care Health Sciences
Radcliffe Observatory Quarter, Woodstock Rd, OX2 6GG
Tel: +44 (0)1865 617 842, Fax: +44 (0)1865 289 412
E-mail: archie@phc.ox.ac.uk Website: www.archiestudy.com

Information and Processing Unit
Area 6
MHRA
151 Buckingham Palace Road
Victoria
SW1W 9SZ

20 Sept 2016

Dear Sir/Madam,

Re: Notice of Substantial Amendment SA014 **Please consider expediting this review**
Study Title: The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a double-blind randomised placebo-controlled trial
CTA number: 215584/0321/001-0001
EudraCT Number: 2013-002822-21
NRES ref: 13/NW/0621
CESP: 391909

Please find enclosed documentation to support our application for approval of a substantial amendment for the above trial. This relates to extending the shelf life of medication to be used in an influenza study and the MHRA helpline suggested we request the review be expedited to allow relabelling before the start of the recruiting season.

Yours sincerely

Tricia Carver
On behalf of Dr Kay Wang, Chief Investigator
Enclosed: Notice of Substantial Amendment SA0014
Proof of payment

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

(●) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Is this a commercially sponsored Phase 1 or Phase 1/2a trial involving healthy volunteers?

( ) Yes (●) No

2b. Will the study involve the use of any medical device without a CE Mark, or a CE marked device which has been modified or will be used outside its intended purposes?

( ) Yes (●) No

2c. Please answer the following question:

Is this trial subject to advice from the Expert Advisory Group on Clinical Trials and the Commission on Human Medicine prior to authorisation from MHRA? ○ Yes ◉ No

2d. Please answer the following question:

Is this a trial of a gene therapy medicinal product? ○ Yes ◉ No

2e. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ○ Yes ◉ No

b) Will you be taking new human tissue samples (or other human biological samples)? ◉ Yes ○ No

c) Will you be using existing human tissue samples (or other human biological samples)? ○ Yes ◉ No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- ☑ England
- ☐ Scotland
- ☐ Wales
- ☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ◉ England
- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Which applications do you require?

IMPORTANT: If your project is taking place in the NHS and is led from England select 'IRAS Form'. If your project is led from Northern Ireland, Scotland or Wales select 'NHS/HSC Research and Development Offices' and/or relevant Research Ethics Committee applications, as appropriate.

- ☐ IRAS Form
- ☑ NHS/HSC Research and Development offices
- ☐ Social Care Research Ethics Committee
- ☑ Research Ethics Committee
- ☑ Medicines and Healthcare products Regulatory Agency (MHRA) – Medicines
- ☐ Gene Therapy Advisory Committee (GTAC)
- ☐ Confidentiality Advisory Group (CAG)
- ☐ National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D Offices in Northern Ireland, Scotland and Wales the CI must create NHS/HSC Site Specific Information forms, for each site, in addition to the study wide forms, and transfer them to the PIs or local collaborators.

For participating NHS organisations in England different arrangements apply for the provision of site specific information. Refer to IRAS Help for more information.

5. Will any research sites in this study be NHS organisations?

(●) Yes ( ) No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out research e.g. NHS Support costs) for this study provided by a NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC), NIHR Patient Safety Translational Research Centre or a Diagnostic Evidence Co-operative in all study sites?

Please see information button for further details.

(●) Yes ( ) No

Please see information button for further details.

6. Do you plan to include any participants who are children?

(●) Yes ( ) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (●) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

( ) Yes (●) No

9. Is the study or any part of it being undertaken as an educational project?

( ) Yes (●) No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

( ) Yes (●) No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

( ) Yes (●) No

SUBSTANTIAL AMENDMENT FORM [1]

NOTIFICATION OF A SUBSTANTIAL AMENDMENT TO A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE EUROPEAN UNION

For official use:

Date of receiving the request:	Grounds for non acceptance/negative opinion:
	Date:
Date of start of procedure:	Authorisation/ positive opinion:
	Date:
Competent authority registration number of the trial:	Withdrawal of amendment application:
Ethics committee registration number of the trial:	Date:

To be filled in by the applicant:

*This form is to be used both for a request to the Competent Authority for authorisation of a **substantial** amendment and to an Ethics Committee for its opinion on a **substantial** amendment. Please indicate the relevant purpose in Section A.*

A TYPE OF NOTIFICATION

A.1 Member State in which the substantial amendment is being submitted:

United Kingdom

A.2 Notification for authorisation to the competent authority: ☑

A.3 Notification for an opinion to the ethics committee: ☐

(1) Cf. Section 3.7.b of the Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (OJ, C82, 30.3.2010, p.1) hereinafter referred to as 'detailed guidance CT-1'.

B TRIAL IDENTIFICATION *(When the amendment concerns more than one trial, repeat this form as necessary.)*

B.1 Does the substantial amendment concern several trials involving the same IMP? [2] ○ Yes ◉ No

B.2 EudraCT number:	2013-002822-21
B.3 Full title of the trial:	The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a double-blind randomised placebo-controlled trial
B.4 Sponsor's protocol code number:	ARCHIE001
B.4 Sponsor's protocol version number:	v2
B.4 Sponsor's protocol date:	12/02/2014

(2) Cf. Section 3.7. of the detailed guidance CT-1

C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

C.1 Sponsor

Organisation:	Univeristy of Oxford
Contact Given name:	Heather
Contact Family name:	House
Address:	Joint Research Office, Block 60, Churchill Hospital
Town/city:	Headington, Oxford
Post code:	OX3 7LE
Telephone:	01865572228
Fax:	
E-mail:	ctrg@admin.ax.ac.uk

C.2 Legal representative [3] of the sponsor in the European Union for the purpose of this trial (if different from the sponsor)

Name of organisation:	
Contact Given name:	
Contact Family name:	
Address:	
Town/city:	
Post code:	
Telephone:	
Fax:	
E-mail:	

(3) As stated in Article 19 of Directive 2001/20/EC.

D APPLICANT IDENTIFICATION, (please tick the appropriate box)

D1. Request for the competent authority

D.1.1 Sponsor	☐
D.1.2 Legal representative of the sponsor	☐
D.1.3 Person or organisation authorised by the sponsor to make the application.	☑

D.1.4 Complete below:

Name of organisation	University of Oxford
Contact Given name	Tricia
Contact Family name	Carver
Address	Nuffield Department of Primary Care Health Sciences
Town/city	Radcliffe Observatory Quarter, Woodstock Road
Post code	OX26GG

Telephone	01865617842
Fax	
E-mail	Tricia.Carver@phc.ox.ac.uk

D2. Request for the Ethics Committee

D.2.1 Sponsor ☐

D.2.2 Legal representative of the sponsor ☐

D.2.3 Person or organisation authorised by the sponsor to make the application. ☐

D.2.4 Investigator in charge of the application if applicable[4]:

- Co-ordinating investigator (for multicentre trial): ☐
- Principal investigator (for single centre trial): ☐

D.2.5 Complete below:

Name of organisation
Given name
Family name
Address
Town/city
Post code
Telephone
Fax
E-mail

(4) According to national legislation.

E SUBSTANTIAL AMENDMENT IDENTIFICATION

E.1 Sponsor's substantial amendment information for the clinical trial concerned:

Code Number: ARCHIE_SA014
Version:
Date: 2016/09/13

E.2 Type of substantial amendment

E.2.1 Amendment to information in the CT application form ○ Yes ◉ No

E.2.2 Amendment to the protocol ○ Yes ◉ No

E.2.3 Amendment to other documents appended to the initial application form ◉ Yes ○ No

If yes specify:
Summary of Product Characteristcs/IMP simplified dossier

E.2.4 Amendment to other documents or information: ○ Yes ◉ No

If yes specify:

E.2.5 This amendment concerns mainly urgent safety measures already implemented[5]: ○ Yes ◉ No

E.2.6 This amendment is to notify a temporary halt of the trial[6]: ○ Yes ◉ No

E.2.7 This amendment is to request the restart of the trial[7]: ○ Yes ◉ No

(5) Cf. Section 3.9. of the detailed guidance CT-1.
(6) Cf. Section 3.10. of the detailed guidance CT-1
(7) Cf. Section 3.10. of the detailed guidance CT-1

E.3 Reasons for the substantial amendment:

E.3.1 Changes in safety or integrity of trial subjects	○ Yes	◉ No
E.3.2 Changes in interpretation of scientific documents/value of the trial	○ Yes	◉ No
E.3.3 Changes in quality of IMP(s)	○ Yes	◉ No
E.3.4 Changes in conduct or management of the trial	◉ Yes	○ No
E.3.5 Change or addition of principal investigator(s), co-ordinating investigator	○ Yes	◉ No
E.3.6 Change/addition of site(s)	○ Yes	◉ No
E.3.7 Other change	○ Yes	◉ No
E.3.7.1 If yes specify:		
E.3.8 Other case	○ Yes	○ No
E.3.8.1 If yes specify:		

E.4 Information on temporary halt of trial:[8]

E.4.1 Date of temporary halt		
E.4.2 Recruitment has been stopped	○ Yes	○ No
E.4.3 Treatment has been stopped	○ Yes	○ No

E.4.4 Number of patients still receiving treatment at time of the temporary halt in the MS concerned by the amendment

E.4.5 Briefly describe:

Justification for a temporary halt of the trial *(free text)*:

The proposed management of patients receiving treatment at time of the halt *(free text)*:

The consequences of the temporary halt for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product *(free text)*:

(8) Cf. Section 3.10. of the detailed guidance CT-1

F DESCRIPTION OF EACH SUBSTANTIAL AMENDMENT[9]

Please use this section to detail each substantial amendment which is being notified. If you are notifying more than one substantial amendment, please use the "Add Amendment" button as required

Substantial amendment 1

Previous and new wording:*(tracked)*
Please see tracked IMP dossier word document

New wording:

Comments/ explanation/ reasons for substantial amendment:
Extension of IMP (both co-amoxiclav and placebo) expiry date based on new data.

(9)Cf. Section 3.7.c. of the detailed guidance CT-1. The sponsor may submit this documentation on a separate sheet.

G CHANGE OF CLINICAL TRIAL SITE(S)/INVESTIGATOR(S) IN THE MEMBER STATE CONCERNED BY THIS AMENDMENT

Type of change:

G.1.1 Addition of a new site

G.1.1.1 Principal investigator (provide details below)

Given name
Middle name(if applicable)
Family name
Qualification (MD...)
Professional address

G.1.2 Removal of an existing site

G.1.2.1 Principal investigator (provide details below)

Given name
Middle name(if applicable)
Family name
Qualification (MD...)
Professional address

G.1.3 Change of co-ordinating investigator (provide details below of the new coordinating investigator)

Given name
Middle name(if applicable)
Family name
Qualification (MD...)
Professional address

G.1.3.6 Indicate the name of the previous co-ordinating investigator:

G.1.4 Change of principal investigator at an existing site (provide details below of the new principal investigator)

Given name
Middle name(if applicable)
Family name
Qualification (MD...)
Professional address

G.1.4.6 Indicate the name of the previous principal investigator:

H CHANGE OF INSTRUCTIONS TO CA FOR FEEDBACK TO SPONSOR

H.1 Change of e-mail contact for feedback on application*

H.2 Change to request to receive an .xml copy of CTA data ○ Yes ◉ No

H.2.1 Do you want a .xml file copy of the CTA form data saved on EudraCT? ○ Yes ◉ No

H.2.1.1 If yes provide the e-mail address(es) to which it should be sent (up to 5 addresses):

H.2.2 Do you want to receive this via password protected link(s)[10]? ○ Yes ◉ No

If you answer no to question H.2.2 the .xml file will be transmitted by less secure e-mail link(s)

H.2.3 Do you want to stop messages to an email for which they were previously requested? ○ Yes ◉ No

H.2.3.1 If yes provide the e-mail address(es) to which feedback should no longer be sent:

(*This will only come into effect from the time at which the request is processed in EudraCT).

(10) This requires a EudraLink account. (See eudract.emea.europa.eu for details)

I LIST OF THE DOCUMENTS APPENDED TO THE NOTIFICATION FORM (cf. Section 3.7 of detailed guidance CT-1)

Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).

I.1 Cover letter ☑

I.2 Extract from the amended document in accordance with Section 3.7.c. of detailed guidance CT-1 (if not contained in Part F of this form) ☐

I.3 Entire new version of the document[11] ☑

I.4 Supporting information ☐

I.5 Revised .xml file and copy of initial application form with amended data highlighted ☐

I.6 Comments on any novel aspect of the amendment if any :

(11) Cf. Section 3.7.c. of the detailed guidance CT-1

J SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).

J.1 I hereby confirm that/ confirm on behalf of the sponsor that (delete which is not applicable)

- The above information given on this request is correct;
- The trial will be conducted according to the protocol, national regulation and the principles of good clinical practice; and
- It is reasonable for the proposed amendment to be undertaken.

J.2 APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY*(as stated in section D.1):* ☐

J.2.1 Signature [12]: .....

J.2.2 Print name:

J.2.3 Date:

This section was signed electronically by Mrs Tricia Carver on 16/09/2016 10:18.

Job Title/Post:

Organisation:

Email: tricia.carver@phc.ox.ac.uk

J.3 APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE *(as stated in section D.2)*: ☐

J.3.1 Signature [13]: .....

J.3.2 Print name:

J.3.3 Date:

(12) On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.
(13) On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.

Sharon Tonner

From: Karen Melham
Sent: 16 September 2016 10:08
To: Tricia Carver; Sharon Tonner
Cc: Research.Portfolio@ouh.nhs.uk
Subject: Sponsor authorisation for substantial amendment 14 to ARCHIE trial

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Tricia
Thank you for sending for our review the amendment proposed to the ARCHIE trial related to extended shelf life of IMP (both co-amoxiclav and placebo) based on new data.
I can confirm that we as sponsor representative are content for this to be sent to the MHRA for review and approval.

Please forward correspondence and any final, REC-approved documents to karl.shepherd@admin.ox.ac.uk to ensure ongoing sponsorship and indemnity.

With best wishes,

Karen

Dr Karen Melham
Senior Clinical Research Support Manager | Clinical Trials & Research Governance (CTRG)
University of Oxford
Joint Research Office, Block 60, Churchill Hospital, Headington, Oxford, OX3 7LE
E: karen.melham@admin.ox.ac.uk **T:** 01865 227093
www.admin.ox.ac.uk/researchsupport

PID:8801-AMD

The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care

ARCHIE

Simplified IMP Dossier

Quality data

Version: 3 (dated 07 September 2016)

Sponsor:
University of Oxford, Joint Research Office, Block 60, Churchill Hospital, Headington, Oxford, OX3 7LE, UK

TABLE OF CONTENTS

Introduction

In ARCHIE, the IMPs are as follow:

IMP	Marketing authorisation holder
70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension	Brown & Burk UK Limited
Placebo to 70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension	N/A

2.2.1.P Investigational Medicinal Product Under Test

According to Article 9(8) of Directive 2001/20/CE of 4 April 2001 and the revised detailed guidance 2010/C 82/01, this section of the IMPD is presented as *simplified IMPD* since part of the supporting documentation has been assessed previously as part of a marketing authorisation in the European Union or in an ICH country.

The MHRA granted Brown & Burk UK Limited marketing authorisation for the medicinal product 70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension (PL 25298/0006) on 16th August 2012.

For this trial, 70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension is manufactured and packaged according to its marketing authorisation. The IMPD quality data for 70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension is therefore constituted by the SmPC for 70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension and the stability data submitted by Micro Labs Limited as part of the product marketing authorisation.

Manufacturer: Micro Labs Limited
16 Veerasandra Industrial Area
Anekal Taluk
Bangalore
Karnataka
IN-560 100
India

No physical modification is being made to the authorised product other than re-labelling of the product label on the bottle and repackaging of bottle into an unbranded secondary carton (See section on Packaging and Labelling).

Stability: Long term stability study (25ºC ± 2ºC & 60% RH ± 5% RH) over a period of 36 months are detailed in Appendix 4. The data showed little change over the 36 months period and the product remained well within the acceptance criteria for all specifications. Based on this data, a shelf life extension to 40 months has been assigned to the product for the ARCHIE trial.

Appendix 1 - Grant of marketing authorisation
Appendix 2 - SmPC
Appendix 3 - Certificate of GMP complicate of manufacturer – Micro Labs Ltd
Appendix 4 - Stability data of Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension (PL 25298/0006)

6.2.1.P Placebo product

6.2.1.P.1 Description and Composition (Placebo)

Placebo to Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension.

6.2.1.P.2 Pharmaceutical Development (Placebo)

Placebo to Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension (70ml) contains the same excipients as the test product. In order to match the test product for fill weight, bulk density, and viscosity, tests were carried out with different excipients ratios in order to identify the most comparable formulation.

6.2.1.P.3 Manufacture

6.2.1.P.3.1 Manufacturer(s) (Placebo)

The placebo is manufactured by the same manufacturer of the test product.

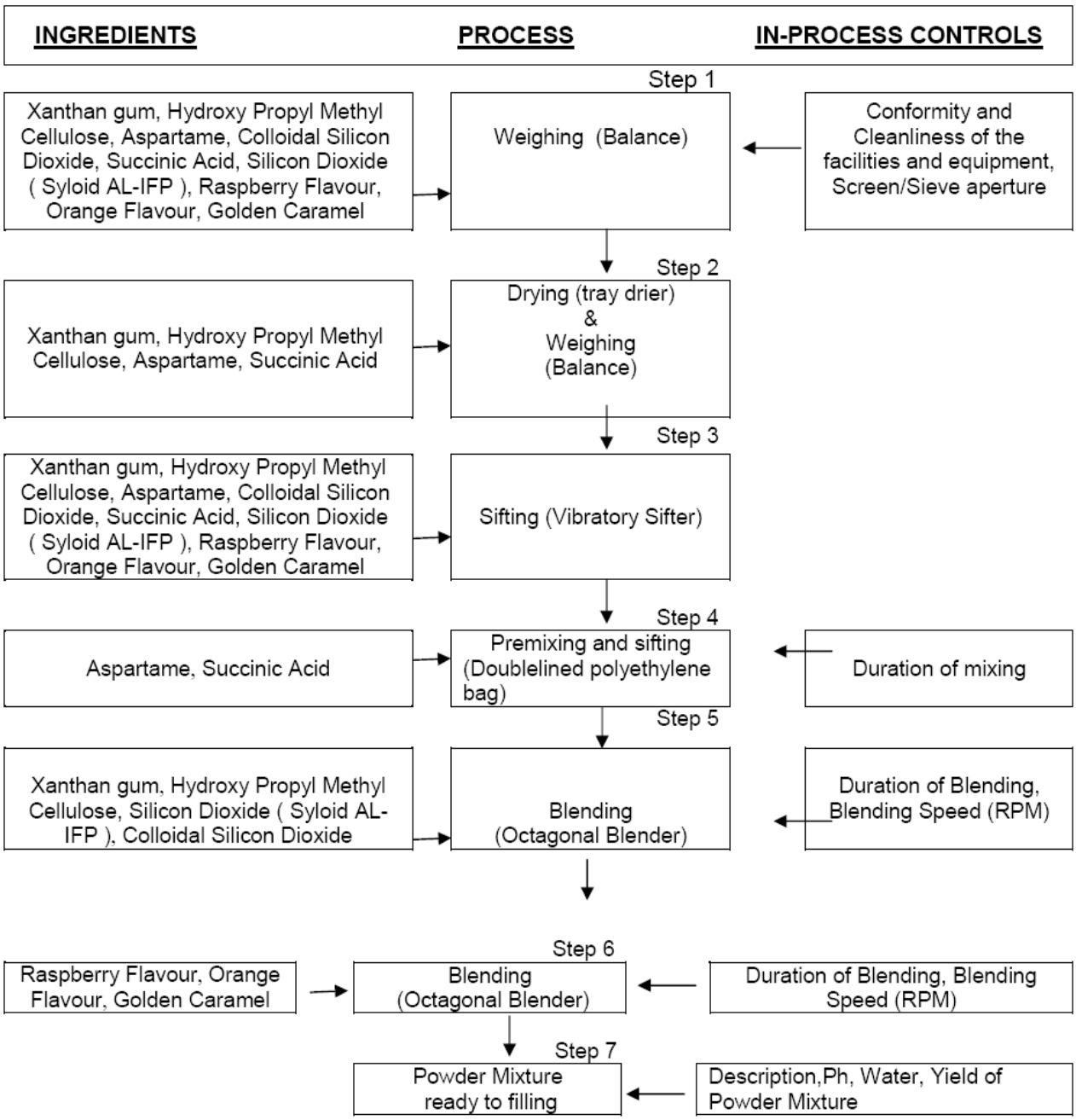
Manufacturer: Micro Labs Limited
16 Veerasandra Industrial Area
Anekal Taluk
Bangalore
Karnataka
IN-560 100
India

Mawdsley-Brooks & Company Limited (MIA(IMP) 741) is responsible for the importation and QP declaration of the placebo comparator.

6.2.1.P.3.2 Batch Formula (Placebo)

Sr. N0.	Ingredients	Grade	Item code	Rationale	Input qty per bottle in g	Overages %	Quantity for the batch (kg)
Dry mixing							
1	Silicon Dioxide (Syloid AL-IFP)	USP/NF	REND 051	Diluent	7.000	NA	45.500
2	Aspartame	Ph. Eur	REND 235	Sweetener	0.500	NA	3.250
3	Succinic Acid	USP/NF	REND 315	PH Adjuster	0.04	NA	0.260
4	Xanthan gum (Ziboxan PM 200)	Ph. Eur	REND 148	Thickener	0.05	NA	0.325
5	Hydroxy Propyl Methyl Cellulose (Methocel E5 LV)	Ph. Eur	REND 234	Thickener	1.200	NA	7.800
6	Colloidal Silicon Dioxide (Cab-o-sil M-5)	Ph. Eur	REND 141	Glidant	1.000	NA	6.500
7	Raspberry Flavour (Raspberry DC 107)	IH	REND 057	Flavour	1.310	NA	8.515
8	Orange Flavour (Orange DC 100 BB)	IH	REND 058	Flavour	1.400	NA	9.100
9	Golden Caramel (Golden Caramel 501118 AP0551)	IH	REND 059	Flavour	1.500	NA	9.750
Total Fill weight					14.00		91.000

6.2.1.P.3.3 Description of Manufacturing Process and Process Controls (Placebo)



6.2.1.P.3.4 Control of Critical Steps and Intermediates (Placebo)

In Process specification:

TEST NO.	TEST	SPECIFICATIONS
1.	Description (In house)	White to off-white powder.
2.	Water content (By KF) (Ph. Eur. method 2.5.12)	Not more than 10 %
3.	pH of the suspension (Ph. Eur. method 2.2.3)	Between 4.3 and 5.3

6.2.1.P.3.5 Process Validation and/or Evaluation (Placebo)

Not applicable

6.2.1.P.4 Control of Excipients (Placebo)

6.2.1.P.4.1 Specifications (Placebo)

Not applicable as all excipients are the same as the test product.

6.2.1.P.4.2 Analytical Procedures (Placebo)

Not applicable as all excipients are the same as the test product.

6.2.1.P.4.3 Validation of Analytical Procedures (Placebo)

Not applicable as all excipients are the same as the test product.

6.2.1.P.4.4 Justification of Specifications (Placebo)

Not applicable as all excipients are of the same as the test product.

6.2.1.P.4.5 Excipients of Animal or Human Origin (Placebo)

Not applicable as all excipients are the same as the test product.

6.2.1.P.4.6 Novel Excipients (Placebo)

There are no novel excipients used in the manufacture of the placebo comparators.

6.2.1.P.5 Control of the Placebo Product (Placebo)

6.2.1.P.5.1 Specifications (Placebo)

SPECIFICATIONS FOR STAGE – I : (INITIAL ANALYSIS)

TEST NO.	TEST	SPECIFICATIONS	
1.	Description (In house) i) Dry powder ii) Reconstituted Suspension	White to off-white powder. White to off-white suspension with fruity aromatic odour.	
2.	Mean mass (In house)	For 70ml pack	14.0 gm ± 5% (Between 13.300 g and 14.700g)
3.	Uniformity of weight (mass) of delivered doses from multidose containers (Ph. Eur. method 2.9.27)	Not more than two of the individual mass deviate from the average mass by more than 10.0 % and none deviates by more than twice the percentage (i.e. 20.0%).	
4.	pH of the suspension (Ph. Eur. method 2.2.3)	Should be between 4.0 and 6.0	
5.	Water content (By KF) (Ph. Eur. method 2.5.12)	Not more than 10 %	
6.	Microbiological quality * (Ph. Eur. method 5.1.4) A) Total Bacterial Count B) Total Fungal Count C) Pathogenic organisms Escherichia coli	 Not more than 1000 CFU / g Not more than 100 CFU / g Should be absent / g	
7.	Reconstitution time (In house)	Not more than 5 minutes.	

* Microbial limit test is monitored only for submission batches and process validation batches, thereafter every 10th batch or first batch of each year.

SPECIFICATIONS FOR STAGE II : RECONSTITUTED SUSPENSION AFTER 7 DAYS*

TEST NO.	TEST	SPECIFICATIONS
1.	Description (In house) Reconstituted suspension:	White to off-white suspension with fruity aromatic odour.
2.	pH of the suspension (Ph. Eur. method 2.2.3)	Should be between 4.0 and 6.0

6.2.1.P.5.2 Analytical Procedures (Placebo)

METHOD OF ANALYSIS

- **Instruction for reconstitution of suspension:**
  Add accurately measured specified quantity of Milli-Q water to each of the bottle. Ensure the constituted solution level is upto the mark available on bottle. Close the cap securely. Shake the bottle vigorously to dissolve the content.

Strength	Pack size (ml)	Reconstitution volume (ml)
400 / 57 mg / 5ml	70	61

1. **Description:**

   a) Dry powder-
   Take a bottle open it on clean butter paper and observe visually against black background. Check the Physical aspects - Colour, lumps, presence of foreign matter etc. and record the observations.

   b) Reconstituted suspension-
   Transfer the sample into a colourless test tube having a inside diameter of 15-25 mm. Make a suspension and observe against a white background for colour and black background for clarity in diffused daylight. Preserve the sample for pH and odour test of suspension.

   Record the observations.

2. **Mean mass:**

   Select 5 containers at random. Weigh the contents of 5 containers and note down the weight in grams up to four decimals. Determine the average mass.

3. **Uniformity of weight (mass) of delivered doses from multidose containers:**

   Weigh individually 20 doses taken at random from one or more containers and determine the individual and average masses.

   Not more than 2 of the individual masses deviate from the average mass by more than 10 per cent and none deviates by more than 20 per cent

4. **pH of the suspension:**

   Adjust the temperature of sample (reconstituted suspension) under test to 25°C ± 2°C.

   Wash the electrode with purified water and blot dry. Immerse the electrode in the sample under test and measure the pH.

   Note the value and report the results.

5. **Water (By Karl Fischer method):**

Transfer an accurately weighed quantity of about 0.5 grams of sample (Dry powder) to the titration flask containing 30ml of anhydrous methanol.

Allow it to disperse for few minutes by stirring. Start the titration with Karl Fischer reagent and continue till the end point is reached. Note down the titer value (V).

Calculate the percent water content using the following formula.

$$\% \text{ Water content} = \frac{\text{Titer value (V) X KF factor X 100}}{\text{Weight of sample taken in mg}}$$

6. **Microbiological quality:**

Refer standard operating procedure for microbiological quality, SOP:QCMB:018

7. **Reconstitution time:**

Select one bottle randomly and tap the bottle lightly to loosen powder. Add half of the specified ml of water and shake well for 1 minute to hydrate the blend. Add rest of the quantity of water and shake well on its longitudinal axis (180°) to form uniform suspension. After interval of 1 minute, open the bottle & physically observe the suspension. Note down the time to form Uniform suspension with out any un-wet particles left.

6.2.1.P.7 Container Closure System (Placebo)

The container closure system for the placebo is the same as the test product.

Primary packaging: HDPE bottle with 28mm polypropylene round CRC cap containing 14g of powder for reconstitution to 70ml.

Secondary packaging: In carton with a 5ml polystyrene syringe dosing device.

6.2.1.P.8 Stability (Placebo)

The placebo product was assigned a provisional shelf life of 24 months in view that both the active and placebo formulations compromise the same excipients and manufactured by the same manufacturer. This has now been extended to 36 months based on ongoing stability testing. Data for the 24 month associated QP certificate is supplied in appendix 5a and 5b.

As per the active, the storage conditions for the placebo formulations will be:

Dry powder: This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

After reconstitution: Store in a refrigerator between 2°C to 8°C in the container supplied and use within 7 days.

Real-time stability study on the placebo product will be carried out at 36 months. If results are compliant to the specifications as listed under section 6.2.1.P.5.1, this shelf-life will be extended accordingly.

Packaging and labelling
Mawdsley-Brooks & Company Limited (MIA(IMP) 741) is responsible for the packaging and labelling of the test products and placebo comparators in a blinded manner. They are also responsible for the batch released and final QP certification of the test products and placebo comparators.

70ml Co-amoxiclav 400mg/57mg/5ml Sugar Free Powder for Oral Suspension

- Commercial label on the HDPE bottle is removed.
- Each bottle is labelled with a blinded Annex 13 label
- Each Annex 13 labelled bottle is placed in an unbranded secondary carton with Annex 13 labelling.
- A 5ml polystyrene syringe dosing device is included in each carton.

Placebo

- Each bottle is labelled with a blinded Annex 13 label.
- Each Annex 13 labelled bottle is placed in an unbranded secondary carton with Annex 13 labelling.
- A 5ml polystyrene syringe dosing device is included in each carton.

Manufacturing site: Unit 22, Quest Park
Wheatley Hall Road
Doncaster
DN2 4LT
UK

Appendix 6 - MIA(IMP) licence – Mawdsley-Brooks & Company Limited

Safeguarding public health

MHRA

Head Of Regulatory Affairs
BROWN & BURK UK LIMITED
5 MARRYAT CLOSE
HOUNSLOW
TW4 5DQ
UNITED KINGDOM

16/08/2012

Dear Head Of Regulatory Affairs,

GRANT / RENEWAL OF MARKETING AUTHORISATION

Our Reference:	PL 25298/0006 - 0001
Your Reference:	25298
Product:	Co amoxiclav 400 mg/57 mg/5 ml Sugar Free Powder for Ora Suspension
Type of Procedure:	Decentralised
Submission Type:	Initial
Submission Category:	Abridged
EU Procedure Number (if applicable):	PT/H/603/02/DC

The Licensing Authority agrees to the grant or renewal of the marketing authorisation for the above submission on the basis of the data provided. This includes any replacement and amendment of the original dossier.

In line with Article 23a of Directive 2001/83/EC as amended, the Marketing Authorisation Holder should submit notification of the actual date of marketing of the product to the Competent Authority.
This notification should be provided by email to the following address: sunsetclause@mhra.gsi.gov.uk.

The formal documents are enclosed. These constitute evidence of authorisation. If you consider them to contain information that is incorrect or not in accordance with the dossier, please return immediately indicating any errors.

All Marketing Authorisations are subject to standard provisions contained in current medicines regulations full details of which are published on the MHRA website:
http://www.mhra.gov.uk/mhra/marketingauthorisationprovisions
Yours sincerely,

Prathibha Madan

The Medicines for Human Use (Marketing Authorisations etc.) Regulations, SI 1994/3144, as amended.

GRANT / RENEWAL OF MARKETING AUTHORISATION

Product: PL 25298/0006 - Co-amoxiclav 400 mg/57 mg/5 ml Sugar Free Powder for Oral Suspension
Submission Type: Initial

Granted to: BROWN & BURK UK LIMITED
5 MARRYAT CLOSE
HOUNSLOW
TW4 5DQ
UNITED KINGDOM

This Marketing Authorisation, under the above reference number is hereby granted / renewed in respect of the product named above. The Summary of Product Characteristics of the product is set out in the attached document.

The application is subject to the further provisions set out or referred to in the above Regulations.

This Marketing Authorisation, as now granted / renewed, unless previously revoked, will continue in force until the expiry date (if applicable) given below.

Grant Date: 16/08/2012

Date of Expiry: 20/06/2017

Pratibha Madan
A person authorised to sign on behalf of the Secretary of State for Health

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Co-amoxiclav 400 mg/57 mg/5 mL Sugar Free Powder for Oral Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Co-amoxiclav Sugar Free Suspension Each 5ml of reconstituted suspension contains 400 mg amoxicillin (as amoxicillin trihydrate) and 57 mg clavulanic acid (as potassium clavulanate).

Excipients:

Co-amoxiclav contains 2.5 mg of aspartame (E951) per ml.

3 PHARMACEUTICAL FORM

Powder for oral suspension.

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Co-amoxiclav is indicated for the treatment of the following infections in adults and children (see sections 4.2, 4.4 and 5.1):

- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis

- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

Doses are expressed throughout in terms of amoxicillin/clavulanic acid content except when doses are stated in terms of an individual component.

The dose of Co-amoxiclav that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to antibacterial agents (see section 4.4)
- The severity and the site of the infection
- The age, weight and renal function of the patient as shown below.

The use of alternative presentations of Co-amoxiclav (e.g. those that provide higher doses of amoxicillin and/or different ratios of amoxicillin to clavulanic acid) should be considered as necessary (see sections 4.4 and 5.1).

For adults and children ≥ 40 kg, this formulation of Co-amoxiclav provides a total daily dose of 1750 mg amoxicillin/ 250 mg clavulanic acid with twice daily dosing and 2625 mg amoxicillin/375 mg clavulanic acid with three times daily dosing, when administered as recommended below. For children < 40 kg, this formulation of Augmentin provides a maximum daily dose of 1000-2800 mg amoxicillin/143-400 mg clavulanic acid, when administered as recommended below. If it is considered that a higher daily dose of amoxicillin is required, it is recommended that another preparation of Co-amoxiclav is selected in order to avoid administration of unnecessarily high daily doses of clavulanic acid (see sections 4.4 and 5.1).

The duration of therapy should be determined by the response of the patient. Some infections (e.g. osteomyelitis) require longer periods of treatment. Treatment should not be extended beyond 14 days without review (see section 4.4 regarding prolonged therapy).

<u>Adults and children ≥ 40 kg</u>

Recommended doses:

- standard dose: (for all indications) 875 mg/125 mg two times a day;
- higher dose - (particularly for infections such as otitis media, sinusitis, lower respiratory tract infections and urinary tract infections): 875 mg/125 mg three times a day.

Children < 40 kg

Children may be treated with Co-amoxiclav tablets, suspensions or paediatric sachets.

Recommended doses:

- 25 mg/3.6 mg/kg/day to 45 mg/6.4 mg/kg/day given as two divided doses;
- up to 70 mg/10 mg/kg/day given as two divided doses may be considered for some infections (such as otitis media, sinusitis and lower respiratory tract infections).

No clinical data are available for Co-amoxiclav 7:1 formulations regarding doses higher than 45 mg/6.4 mg per kg per day in children under 2 years

There are no clinical data for Co-amoxiclav 7:1 formulations for patients under 2 months of age. Dosing recommendations in this population therefore cannot be made.

Elderly

No dose adjustment is considered necessary.

Renal impairment

No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

In patients with creatinine clearance less than 30 ml/min, the use of Co-amoxiclav presentations with an amoxicillin to clavulanic acid ratio of 7:1 is not recommended, as no recommendations for dose adjustments are available.

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals (see sections 4.3 and 4.4).

Method of administration

Co-amoxiclav is for oral use.

Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption of amoxicillin/clavulanic acid.

Therapy can be started parenterally according to the SmPC of the IV-formulation and continued with an oral preparation.

Shake to loosen powder, add water as directed, invert and shake.
Shake the bottle before each dose (see section 6.6 and 12).

4.3 Contraindications

Hypersensitivity to the active substances, to any of the penicillins or to any of the excipients listed in section 6.1.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid (see section 4.8).

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin/clavulanic acid therapy must be discontinued and appropriate alternative therapy instituted.

In the case that an infection is proven to be due to an amoxicillin-susceptible organisms(s), consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance.

This presentation of Co-amoxiclav is not suitable for use when there is a high risk that the presumptive pathogens have resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. This presentation should not be used to treat penicillin-resistant S. pneumoniae.

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see 4.8).

Amoxicillin/clavulanic acid should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustulae may be a symptom of acute generalised exanthemous pustulosis (AGEP) (see Section 4.8). This reaction requires Co-amoxiclav discontinuation and contra-indicates any subsequent administration of amoxicillin.

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment (see sections 4.2, 4.3 and 4.8).

Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. In all populations, signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects (see section 4.8).

Antibiotic-associated colitis has been reported with nearly all antibacterial agents including amoxicillin and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of any antibiotics. Should antibiotic-associated colitis occur, Co-amoxiclav should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic drugs are contra-indicated in this situation.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin/clavulanic acid. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5 and 4.8).

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.9).

During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of clavulanic acid in Co-amoxiclav may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

There have been reports of positive test results using the Bio-Rad Laboratories Platelia *Aspergillus* EIA test in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of *Aspergillus* infection. Cross-reactions with non- *Aspergillus* polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia *Aspergillus* EIA test have been reported. Therefore, positive test results in patients receiving amoxicillin/clavulanic acid should be interpreted cautiously and confirmed by other diagnostic methods.

Co-amoxiclav contains 2.5 mg of aspartame (E951) per ml, a source of phenylalanine.

This medicine should be used with caution in patients with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

4.6 Pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). Limited data on the use of amoxicillin/clavulanic acid during pregnancy in humans do not indicate an increased risk of congenital malformations. In a single study in women with preterm, premature rupture of the foetal membrane it was reported that prophylactic treatment with amoxicillin/clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates. Use should be avoided during pregnancy, unless considered essential by the physician.

Breastfeeding

Both substances are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breast-fed infant). Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxicillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.

The ADRs sorted by MedDRA System Organ Class are listed below.

The following terminologies have been used in order to classify the occurrence of undesirable effects.

Very common (≥ 1/10)

Common (≥ 1/100 to <1/10)

Uncommon (≥ 1/1,000 to <1/100)

Rare (≥ 1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

Infections and infestations	
Mucocutaneous candidosis	Common
Overgrowth of non-susceptible organisms	Not known
Blood and lymphatic system disorders	
Reversible leucopenia (including neutropenia)	Rare
Thrombocytopenia	Rare
Reversible agranulocytosis	Not known
Haemolytic anaemia	Not known
Prolongation of bleeding time and prothrombin time[1]	Not known
Immune system disorders[10]	
Angioneurotic oedema	Not known
Anaphylaxis	Not known
Serum sickness-like syndrome	Not known

Hypersensitivity vasculitis	Not known
Nervous system disorders	
Dizziness	Uncommon
Headache	Uncommon
Reversible hyperactivity	Not known
Convulsions[2]	Not known
Gastrointestinal disorders	
Diarrhoea	Common
Nausea[3]	Common
Vomiting	Common
Indigestion	Uncommon
Antibiotic-associated colitis[4]	Not known
Black hairy tongue	Not known
Tooth discolouration[11]	Not known
Hepatobiliary disorders	
Rises in AST and/or ALT[5]	Uncommon
Hepatitis[6]	Not known
Cholestatic jaundice[6]	Not known
Skin and subcutaneous tissue disorders [7]	
Skin rash	Uncommon
Pruritus	Uncommon
Urticaria	Uncommon
Erythema multiforme	Rare
Stevens-Johnson syndrome	Not known
Toxic epidermal necrolysis	Not known
Bullous exfoliative-dermatitis	Not known
Acute generalised exanthemous pustulosis (AGEP)[9]	Not known

Renal and urinary disorders	
Interstitial nephritis	Not known
Crystalluria[8]	Not known

[1] See section 4.4

[2] See section 4.4

[3] Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, they may be reduced by taking Co-amoxiclav at the start of a meal.

[4] Including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)

[5] A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.

[6] These events have been noted with other penicillins and cephalosporins (see section 4.4).

[7] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).

[8] See section 4.9

[9] See section 4.3

[10] See section 4.4

[11] Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

4.9 Overdose

Symptoms and signs of overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained (see section 4.4)

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors; ATC code: J01CR02.

Mechanism

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

PK/PD relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The two main mechanisms of resistance to amoxicillin/clavulanic acid are:

• Inactivation by those bacterial beta-lactamases that are not themselves inhibited by clavulanic acid, including class B, C and D.

• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin/clavulanic acid are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)

Organism	Susceptibility Breakpoints (µg/ml)		
	Susceptible	Intermediate	Resistant
Haemophilus influenzae[1]	≤ 1	-	> 1
Moraxella catarrhalis[1]	≤ 1	-	> 1
Staphylococcus aureus[2]	≤ 2	-	> 2
Coagulase-negative staphylococci[2]	≤ 0.25		> 0.25
Enterococcus[1]	≤ 4	8	> 8
Streptococcus A, B, C, G[5]	≤ 0.25	-	> 0.25
Streptococcus pneumoniae[3]	≤ 0.5	1-2	> 2
Enterobacteriaceae[1,4]	-	-	> 8

Gram-negative Anaerobes[1]	≤ 4	8	> 8
Gram-positive Anaerobes[1]	≤ 4	8	> 8
Non-species related breakpoints[1]	≤ 2	4-8	> 8

[1] The reported values are for Amoxicillin concentrations. For susceptibility testing purposes, the concentration of Clavulanic acid is fixed at 2 mg/l.

[2] The reported values are Oxacillin concentrations.

[3] Breakpoint values in the table are based on Ampicillin breakpoints.

[4] The resistant breakpoint of R>8 mg/l ensures that all isolates with resistance mechanisms are reported resistant.

[5] Breakpoint values in the table are based on Benzylpenicillin breakpoints.

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobic Gram-positive micro-organisms
Enterococcus faecalis
Gardnerella vaginalis
Staphylococcus aureus (methicillin-susceptible)
Streptococcus agalactiae

Streptococcus pneumoniae[1]
Streptococcus pyogenes and other beta-haemolytic streptococci
Streptococcus viridans group
Aerobic Gram-negative micro-organisms
Capnocytophaga spp.
Eikenella corrodens
Haemophilus influenzae[2]
Moraxella catarrhalis
Pasteurella multocida
Anaerobic micro-organisms
Bacteroides fragilis
Fusobacterium nucleatum
Prevotella spp.
Species for which acquired resistance may be a problem
Aerobic Gram-positive micro-organisms
Enterococcus faecium $
Aerobic Gram-negative micro-organisms
Escherichia coli

Klebsiella oxytoca *Klebsiella pneumoniae* *Proteus mirabilis* *Proteus vulgaris*
Inherently resistant organisms
Aerobic Gram-negative micro-organisms *Acinetobacter* sp. *Citrobacter freundii* *Enterobacter* sp. *Legionella pneumophila* *Morganella morganii* *Providencia* spp. *Pseudomonas* sp. *Serratia* sp. *Stenotrophomonas maltophilia* Other micro-organisms *Chlamydophila pneumoniae*

Chlamydophila psittaci *Coxiella burnetti* *Mycoplasma pneumoniae*
[S] Natural intermediate susceptibility in the absence of acquired mechanism of resistance. [£] All methicillin-resistant staphylococci are resistant to amoxicillin/clavulanic acid [1]*Streptococcus pneumoniae* that are resistant to penicillin should not be treated with this presentation of amoxicillin/clavulanic acid (see sections 4.2 and 4.4). [2] Strains with decreased susceptibility have been reported in some countries in the EU with a frequency higher than 10%.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin and clavulanic acid, are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (T_{max}) in each case is approximately one hour.

The pharmacokinetic results for a study, in which amoxicillin/clavulanic acid (875 mg/125 mg tablets given twice daily) was administered in the fasting state to groups of healthy volunteers are presented below.

Mean (± SD) pharmacokinetic parameters					
Active substance(s) administered	Dose (mg)	C_{max} (µg/ml)	T_{max} * (h)	$AUC_{(0-24h)}$ (µg.h/ml)	T 1/2 (h)

Amoxicillin					
AMX/CA 875 mg/125 mg	875	11.64 ± 2.78	1.50 (1.0-2.5)	53.52 ± 12.31	1.19 ± 0.21
Clavulanic acid					
AMX/CA 875 mg/125 mg	125	2.18 ± 0.99	1.25 (1.0-2.0)	10.16 ± 3.04	0.96 ± 0.12

AMX – amoxicillin, CA – clavulanic acid

*Median (range)

Amoxicillin and clavulanic acid serum concentrations achieved with amoxicillin/clavulanic acid are similar to those produced by the oral administration of equivalent doses of amoxicillin or clavulanic acid alone.

Distribution

About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0.3-0.4 l/kg for amoxicillin and around 0.2 l/kg for clavulanic acid.

Following intravenous administration, both amoxicillin and clavulanic acid have been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is no evidence for significant tissue retention of drug-derived material for either component. Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanic acid can also be detected in breast milk (see section 4.6).

Both amoxicillin and clavulanic acid have been shown to cross the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose. Clavulanic acid is extensively metabolized in man and eliminated in urine and faeces and as carbon dioxide in expired air.

Elimination

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and nonrenal mechanisms.

Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/h in healthy subjects. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of single Co-amoxiclav 250 mg/125 mg or 500 mg/125 mg tablets. Various studies have found the urinary excretion to be 50-85% for amoxicillin and between 27-60% for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.

Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid (see section 4.5).

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender

Following oral administration of amoxicillin/clavulanic acid to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of either amoxicillin or clavulanic acid.

Renal impairment

The total serum clearance of amoxicillin/clavulanic acid decreases proportionately with decreasing renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid (see section 4.2).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

Repeat dose toxicity studies performed in dogs with amoxicillin/clavulanic acid demonstrate gastric irritancy and vomiting, and discoloured tongue.

Carcinogenicity studies have not been conducted with Co-amoxiclav or its components.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silicon Dioxide (E551)

Aspartame (E951)

Succinic acid (E363)

Xanthan Gum (E415)

Hypromellose (E464)

Colloidal anhydrous silica (E551)

Raspberry Flavour [Acacia gum (E414), Nature identical flavouring substance, Propylene glycol (E1520), Artificial flavouring substance and Flavouring preparation]

Orange Flavour [Acacia gum (E414), Flavouring preparation and Butylated hydroxyanisole (E320)]

Golden Caramel [Maltodextrin, Triethyl Citrate (E1505), Artificial Flavours and Acetic acid (E260)]

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

Dry powder: 2 Years

Reconstituted suspension: 7 days, when stored between 2°C to 8°C

6.4 Special precautions for storage

Dry powder: This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

After reconstitution: Store in a refrigerator between 2°C to 8°C in the container supplied and use within 7 days.

6.5 Nature and contents of container

Presentation 1: 5ml polystyrene syringe dosing device supplied in carton

Presentation 2: No syringe dosing device supplied in carton

HDPE bottle with 28mm polypropylene round CRC cap containing 6g, 12g, 14g and 20g of powder for reconstitution to 30ml, 60ml, 70ml and 100ml respectively.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

Check cap seal is intact before using. Shake bottle to loosen powder. Add volume of water (as indicated below) invert and shake well.

Volume of water to be added at reconstitution (ml)	Final volume of reconstituted oral suspension (ml)
25 ml	30 ml
56 ml	60 ml
61 ml	70 ml
87 ml	100 ml

Any unused medicinal product or waste should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Brown & Burk UK Limited
5 Marryat Close
Hounslow West
Middlesex
TW4 5DQ
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 25298/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/08/2012

10 DATE OF REVISION OF THE TEXT

16/08/2012

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Co-amoxiclav 400 mg/57 mg/5 mL Sugar Free Powder for Oral Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Co-amoxiclav Sugar Free Suspension Each 5ml of reconstituted suspension contains 400 mg amoxicillin (as amoxicillin trihydrate) and 57 mg clavulanic acid (as potassium clavulanate).

Excipients:

Co-amoxiclav contains 2.5 mg of aspartame (E951) per ml.

3 PHARMACEUTICAL FORM

Powder for oral suspension.

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Co-amoxiclav is indicated for the treatment of the following infections in adults and children (see sections 4.2, 4.4 and 5.1):

- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

Doses are expressed throughout in terms of amoxicillin/clavulanic acid content except when doses are stated in terms of an individual component.

The dose of Co-amoxiclav that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to antibacterial agents (see section 4.4)
- The severity and the site of the infection
- The age, weight and renal function of the patient as shown below.

The use of alternative presentations of Co-amoxiclav (e.g. those that provide higher doses of amoxicillin and/or different ratios of amoxicillin to clavulanic acid) should be considered as necessary (see sections 4.4 and 5.1).

For adults and children ≥ 40 kg, this formulation of Co-amoxiclav provides a total daily dose of 1750 mg amoxicillin/ 250 mg clavulanic acid with twice daily dosing and 2625 mg amoxicillin/375 mg clavulanic acid with three times daily dosing, when administered as recommended below. For children < 40 kg, this formulation of Augmentin provides a maximum daily dose of 1000-2800 mg amoxicillin/143-400 mg clavulanic acid, when administered as recommended below. If it is considered that a higher daily dose of amoxicillin is required, it is recommended that another preparation of Co-amoxiclav is selected in order to avoid administration of unnecessarily high daily doses of clavulanic acid (see sections 4.4 and 5.1).

The duration of therapy should be determined by the response of the patient. Some infections (e.g. osteomyelitis) require longer periods of treatment. Treatment should not be extended beyond 14 days without review (see section 4.4 regarding prolonged therapy).

<u>Adults and children ≥ 40 kg</u>

Recommended doses:

- standard dose: (for all indications) 875 mg/125 mg two times a day;
- higher dose - (particularly for infections such as otitis media, sinusitis, lower respiratory tract infections and urinary tract infections): 875 mg/125 mg three times a day.

Children < 40 kg

Children may be treated with Co-amoxiclav tablets, suspensions or paediatric sachets.

Recommended doses:

- 25 mg/3.6 mg/kg/day to 45 mg/6.4 mg/kg/day given as two divided doses;
- up to 70 mg/10 mg/kg/day given as two divided doses may be considered for some infections (such as otitis media, sinusitis and lower respiratory tract infections).

No clinical data are available for Co-amoxiclav 7:1 formulations regarding doses higher than 45 mg/6.4 mg per kg per day in children under 2 years

There are no clinical data for Co-amoxiclav 7:1 formulations for patients under 2 months of age. Dosing recommendations in this population therefore cannot be made.

Elderly

No dose adjustment is considered necessary.

Renal impairment

No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

In patients with creatinine clearance less than 30 ml/min, the use of Co-amoxiclav presentations with an amoxicillin to clavulanic acid ratio of 7:1 is not recommended, as no recommendations for dose adjustments are available.

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals (see sections 4.3 and 4.4).

Method of administration

Co-amoxiclav is for oral use.

Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption of amoxicillin/clavulanic acid.

Therapy can be started parenterally according to the SmPC of the IV-formulation and continued with an oral preparation.

Shake to loosen powder, add water as directed, invert and shake.
Shake the bottle before each dose (see section 6.6 and 12).

4.3 Contraindications

Hypersensitivity to the active substances, to any of the penicillins or to any of the excipients listed in section 6.1.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid (see section 4.8).

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin/clavulanic acid therapy must be discontinued and appropriate alternative therapy instituted.

In the case that an infection is proven to be due to an amoxicillin-susceptible organisms(s), consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance.

This presentation of Co-amoxiclav is not suitable for use when there is a high risk that the presumptive pathogens have resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. This presentation should not be used to treat penicillin-resistant S. pneumoniae.

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see 4.8).

Amoxicillin/clavulanic acid should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustulae may be a symptom of acute generalised exanthemous pustulosis (AGEP) (see Section 4.8). This reaction requires Co-amoxiclav discontinuation and contra-indicates any subsequent administration of amoxicillin.

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment (see sections 4.2, 4.3 and 4.8).

Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. In all populations, signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects (see section 4.8).

Antibiotic-associated colitis has been reported with nearly all antibacterial agents including amoxicillin and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of any antibiotics. Should antibiotic-associated colitis occur, Co-amoxiclav should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic drugs are contra-indicated in this situation.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin/clavulanic acid. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5 and 4.8).

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.9).

During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of clavulanic acid in Co-amoxiclav may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

There have been reports of positive test results using the Bio-Rad Laboratories Platelia *Aspergillus* EIA test in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of *Aspergillus* infection. Cross-reactions with non- *Aspergillus* polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia *Aspergillus* EIA test have been reported. Therefore, positive test results in patients receiving amoxicillin/clavulanic acid should be interpreted cautiously and confirmed by other diagnostic methods.

Co-amoxiclav contains 2.5 mg of aspartame (E951) per ml, a source of phenylalanine.

This medicine should be used with caution in patients with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

4.6 Pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). Limited data on the use of amoxicillin/clavulanic acid during pregnancy in humans do not indicate an increased risk of congenital malformations. In a single study in women with preterm, premature rupture of the foetal membrane it was reported that prophylactic treatment with amoxicillin/clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates. Use should be avoided during pregnancy, unless considered essential by the physician.

Breastfeeding

Both substances are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breast-fed infant). Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxicillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.

The ADRs sorted by MedDRA System Organ Class are listed below.

The following terminologies have been used in order to classify the occurrence of undesirable effects.

Very common (≥ 1/10)

Common (≥ 1/100 to <1/10)

Uncommon (≥ 1/1,000 to <1/100)

Rare (≥ 1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

Infections and infestations	
Mucocutaneous candidosis	Common
Overgrowth of non-susceptible organisms	Not known
Blood and lymphatic system disorders	
Reversible leucopenia (including neutropenia)	Rare
Thrombocytopenia	Rare
Reversible agranulocytosis	Not known
Haemolytic anaemia	Not known
Prolongation of bleeding time and prothrombin time[1]	Not known
Immune system disorders[10]	
Angioneurotic oedema	Not known
Anaphylaxis	Not known
Serum sickness-like syndrome	Not known

Hypersensitivity vasculitis	Not known
Nervous system disorders	
Dizziness	Uncommon
Headache	Uncommon
Reversible hyperactivity	Not known
Convulsions[2]	Not known
Gastrointestinal disorders	
Diarrhoea	Common
Nausea[3]	Common
Vomiting	Common
Indigestion	Uncommon
Antibiotic-associated colitis[4]	Not known
Black hairy tongue	Not known
Tooth discolouration[11]	Not known
Hepatobiliary disorders	
Rises in AST and/or ALT[5]	Uncommon
Hepatitis[6]	Not known
Cholestatic jaundice[6]	Not known
Skin and subcutaneous tissue disorders [7]	
Skin rash	Uncommon
Pruritus	Uncommon
Urticaria	Uncommon
Erythema multiforme	Rare
Stevens-Johnson syndrome	Not known
Toxic epidermal necrolysis	Not known
Bullous exfoliative-dermatitis	Not known
Acute generalised exanthemous pustulosis (AGEP)[9]	Not known
Renal and urinary disorders	
Interstitial nephritis	Not known
Crystalluria[8]	Not known

[1] See section 4.4

[2] See section 4.4

[3] Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, they may be reduced by taking Co-amoxiclav at the start of a meal.

[4] Including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)

[5] A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.

[6] These events have been noted with other penicillins and cephalosporins (see section 4.4).

[7] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).

[8] See section 4.9

[9] See section 4.3

[10] See section 4.4

[11] Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

4.9 Overdose

Symptoms and signs of overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained (see section 4.4)

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors; ATC code: J01CR02.

Mechanism

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

PK/PD relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The two main mechanisms of resistance to amoxicillin/clavulanic acid are:

• Inactivation by those bacterial beta-lactamases that are not themselves inhibited by clavulanic acid, including class B, C and D.

• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin/clavulanic acid are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)

Organism	Susceptibility Breakpoints (µg/ml)		
	Susceptible	Intermediate	Resistant
Haemophilus influenzae[1]	≤ 1	-	> 1
Moraxella catarrhalis[1]	≤ 1	-	> 1
Staphylococcus aureus [2]	≤ 2	-	> 2
Coagulase-negative staphylococci [2]	≤ 0.25		> 0.25
Enterococcus[1]	≤ 4	8	> 8
Streptococcus A, B, C, G[5]	≤ 0.25	-	> 0.25
Streptococcus pneumoniae[3]	≤ 0.5	1-2	> 2
Enterobacteriaceae[1,4]	-	-	> 8

Gram-negative Anaerobes[1]	≤ 4	8	> 8
Gram-positive Anaerobes[1]	≤ 4	8	> 8
Non-species related breakpoints[1]	≤ 2	4-8	> 8

[1] The reported values are for Amoxicillin concentrations. For susceptibility testing purposes, the concentration of Clavulanic acid is fixed at 2 mg/l.

[2] The reported values are Oxacillin concentrations.

[3] Breakpoint values in the table are based on Ampicillin breakpoints.

[4] The resistant breakpoint of R>8 mg/l ensures that all isolates with resistance mechanisms are reported resistant.

[5] Breakpoint values in the table are based on Benzylpenicillin breakpoints.

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobic Gram-positive micro-organisms
Enterococcus faecalis
Gardnerella vaginalis
Staphylococcus aureus (methicillin-susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae[1]
Streptococcus pyogenes and other beta-haemolytic streptococci
Streptococcus viridans group
Aerobic Gram-negative micro-organisms
Capnocytophaga spp.
Eikenella corrodens
Haemophilus influenzae[2]
Moraxella catarrhalis
Pasteurella multocida
Anaerobic micro-organisms
Bacteroides fragilis
Fusobacterium nucleatum
Prevotella spp.
Species for which acquired resistance may be a problem
Aerobic Gram-positive micro-organisms
Enterococcus faecium $
Aerobic Gram-negative micro-organisms
Escherichia coli

Klebsiella oxytoca *Klebsiella pneumoniae* *Proteus mirabilis* *Proteus vulgaris*
Inherently resistant organisms
Aerobic Gram-negative micro-organisms *Acinetobacter* sp. *Citrobacter freundii* *Enterobacter* sp. *Legionella pneumophila* *Morganella morganii* *Providencia* spp. *Pseudomonas* sp. *Serratia* sp. *Stenotrophomonas maltophilia* Other micro-organisms *Chlamydophila pneumoniae* *Chlamydophila psittaci* *Coxiella burnetti* *Mycoplasma pneumoniae*
[$] Natural intermediate susceptibility in the absence of acquired mechanism of resistance. [£] All methicillin-resistant staphylococci are resistant to amoxicillin/clavulanic acid [1]*Streptococcus pneumoniae* that are resistant to penicillin should not be treated with this presentation of amoxicillin/clavulanic acid (see sections 4.2 and 4.4). [2] Strains with decreased susceptibility have been reported in some countries in the EU with a frequency higher than 10%.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin and clavulanic acid, are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (T_{max}) in each case is approximately one hour.

The pharmacokinetic results for a study, in which amoxicillin/clavulanic acid (875 mg/125 mg tablets given twice daily) was administered in the fasting state to groups of healthy volunteers are presented below.

Mean (± SD) pharmacokinetic parameters					
Active substance(s) administered	Dose (mg)	C_{max} (µg/ml)	T_{max} * (h)	AUC $_{(0-24h)}$ (µg.h/ml)	T 1/2 (h)

Amoxicillin					
AMX/CA 875 mg/125 mg	875	11.64 ± 2.78	1.50 (1.0-2.5)	53.52 ± 12.31	1.19 ± 0.21
Clavulanic acid					
AMX/CA 875 mg/125 mg	125	2.18 ± 0.99	1.25 (1.0-2.0)	10.16 ± 3.04	0.96 ± 0.12

AMX – amoxicillin, CA – clavulanic acid

*Median (range)

Amoxicillin and clavulanic acid serum concentrations achieved with amoxicillin/clavulanic acid are similar to those produced by the oral administration of equivalent doses of amoxicillin or clavulanic acid alone.

Distribution

About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0.3-0.4 l/kg for amoxicillin and around 0.2 l/kg for clavulanic acid.

Following intravenous administration, both amoxicillin and clavulanic acid have been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is no evidence for significant tissue retention of drug-derived material for either component. Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanic acid can also be detected in breast milk (see section 4.6).

Both amoxicillin and clavulanic acid have been shown to cross the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose. Clavulanic acid is extensively metabolized in man and eliminated in urine and faeces and as carbon dioxide in expired air.

Elimination

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and nonrenal mechanisms.

Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/h in healthy subjects. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of single Co-amoxiclav 250 mg/125 mg or 500 mg/125 mg tablets. Various studies have found the urinary excretion to be 50-85% for amoxicillin and between 27-60% for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.

Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid (see section 4.5).

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender

Following oral administration of amoxicillin/clavulanic acid to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of either amoxicillin or clavulanic acid.

Renal impairment

The total serum clearance of amoxicillin/clavulanic acid decreases proportionately with decreasing renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid (see section 4.2).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

Repeat dose toxicity studies performed in dogs with amoxicillin/clavulanic acid demonstrate gastric irritancy and vomiting, and discoloured tongue.

Carcinogenicity studies have not been conducted with Co-amoxiclav or its components.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silicon Dioxide (E551)

Aspartame (E951)

Succinic acid (E363)

Xanthan Gum (E415)

Hypromellose (E464)

Colloidal anhydrous silica (E551)

Raspberry Flavour [Acacia gum (E414), Nature identical flavouring substance, Propylene glycol (E1520), Artificial flavouring substance and Flavouring preparation]

Orange Flavour [Acacia gum (E414), Flavouring preparation and Butylated hydroxyanisole (E320)]

Golden Caramel [Maltodextrin, Triethyl Citrate (E1505), Artificial Flavours and Acetic acid (E260)]

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

Dry powder: 3 Years

Reconstituted suspension: 7 days, when stored between 2°C to 8°C

6.4 Special precautions for storage

Dry powder: This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

After reconstitution: Store in a refrigerator between 2°C to 8°C in the container supplied and use within 7 days.

6.5 Nature and contents of container

Presentation 1: 5ml polystyrene syringe dosing device supplied in carton

Presentation 2: No syringe dosing device supplied in carton

HDPE bottle with 28mm polypropylene round CRC cap containing 6g, 12g, 14g and 20g of powder for reconstitution to 30ml, 60ml, 70ml and 100ml respectively.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

White to off-white powder which on reconstitution with water gives white to off-white suspension with fruity aromatic odor

Check cap seal is intact before using. Shake bottle to loosen powder. Add volume of water (as indicated below) invert and shake well.

Volume of water to be added at reconstitution (ml)	Final volume of reconstituted oral suspension (ml)
25 ml	30 ml
56 ml	60 ml
61 ml	70 ml
87 ml	100 ml

Any unused medicinal product or waste should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Brown & Burk UK Limited
5 Marryat Close
Hounslow West
Middlesex
TW4 5DQ
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 25298/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/08/2012

10 DATE OF REVISION OF THE TEXT

11/04/2014

Appendix 3 MHRA Certificate 13-Oct-14

MHRA
Regulating Medicines and Medical Devices

MHRA
151 Buckingham Palace Road
London SW1W 9SZ
United Kingdom

mhra.gov.uk

RESTRICTED – COMMERCIAL
Mr S M Mudda
MICRO LABS LIMITED
16 VEERASANDRA INDUSTRIAL AREA
ANEKAL TALUK
BANGALORE
KARNATAKA
IN-560 100
INDIA

Medicines and Healthcare
Products Regulatory Agency

Certificate No: UK GMP 22481 Insp GMP 22481/366976-0004

MHRA
Regulating Medicines and Medical Devices

Medicines and Healthcare products Regulatory Agency

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with Art. 111(5) of Directive 2001/83/EC.

The competent authority of the United Kingdom confirms the following:

The manufacturer	MICRO LABS LIMITED
Site address	16 VEERASANDRA INDUSTRIAL AREA ANEKAL TALUK BANGALORE KARNATAKA IN-560 100 INDIA

Has been inspected in connection with marketing authorisation(s) listing manufacturers located outside of the European Economic Area in accordance with Art.111(4) of Directive 2001/83/EC transposed in the following national legislation: The Human Medicines Regulations 2012 (SI 2012/1916).

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 13/10/2014, it is considered that it complies with the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field.

This certificate is only valid when presented with all pages and both parts 1 and 2.

The authenticity of this certificate may be verified in EudraGMDP. If it does not appear please contact the issuing authority.

MHRA
Regulating Medicines and Medical Devices

Part 2

Human Medicinal Products

1. MANUFACTURING OPERATIONS

1.1 Sterile products

Not Authorised

1.2 Non-sterile products

1.2.1 Non-sterile products (processing operations for the following dosage forms)

1.2.1.1 Capsules, hard shell
1.2.1.13 Tablets
1.2.1.17 Other non-sterile medicinal products
Oral powder for reconstruction

1.3 Biological medicinal products

Not Authorised

1.4 Other products or manufacturing activity

Not Authorised

1.5 Packaging

1.5.2 Secondary packaging

1.6 Quality control testing

1.6.2 Microbiological: non-sterility
1.6.3 Chemical/physical

2. IMPORTATION OF MEDICINAL PRODUCTS

2.1 Quality control testing of imported medicinal products

Not Authorised

2.2 Batch certification of imported medicinal products

Not Authorised

2.3 Other importation activities

Not Authorised

MHRA
Regulating Medicines and Medical Devices

3. MANUFACTURING OPERATIONS

3.1 Manufacture of Active Substance by Chemical Synthesis
Not Authorised

3.2 Processing Activities of Active Substance from Natural Sources
Not Authorised

3.3 Manufacture of Active Substance using Biological Processes
Not Authorised

3.4 Manufacture of sterile active substance
Not Authorised

3.5 General Finishing Steps
Not Authorised

3.6 Quality Control Testing
Not Authorised

4 Other Activities
Not Authorised

MHRA
Regulating Medicines and Medical Devices

Any restrictions or clarifying remarks related to the scope of this certificate:

ML11 Authorised only.

1. Building(s)/Area(s)

   N/A

2. Room(s)

   N/A

3. Line(s) Equipment(s)

   N/A

4. QC testing

   N/A

5. Medicinal Product(s)/IMP(s)

   N/A

Name of the authorised person of the Competent Authority of the United Kingdom

Tracy Lovatt
GMP Inspector
Tracy.Lovatt@mhra.gsi.gov.uk

Date: 10/08/2015

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

3.2 : Body of Data

3.2.P : DRUG PRODUCT
(Co-amoxiclav 200/28.5mg/5ml, 400/57mg/5ml Powder for Oral Suspension)

3.2.P.8 : Stability
(Co-amoxiclav 200/28.5mg/5ml, 400/57mg/5ml Powder for Oral Suspension)

3.2.P.8.3 : Stability Data
(Co-amoxiclav 200/28.5mg/5ml, 400/57mg/5ml Powder for Oral Suspension)

Two submission batches of Co-amoxiclav 200/28.5mg/5ml and 400/57mg/5ml Powder for Oral Suspension were manufactured and packed in volume of 30 ml, 60 ml, 70 ml and 100 ml respectively. These filled HDPE Bottles were charged for the stability studies in simulated marketed packs. Details about stability studies of submission batches are described as follows;

Stability study program and schedule details:

Stability study	Stability conditions		Frequency of testing
	Temperature	Humidity	
Accelerated condition	40ºC ± 2ºC	75% RH ± 5% RH	Initial, 1, 2, 3 & 6 months
Long Term condition	25ºC ± 2ºC	60% RH ± 5% RH	Initial, 3, 6, 9, 12, 18, 24 and 36 months
Intermediate condition *	30ºC ± 2ºC	65% RH ± 5% RH	Initial,1,2, 3, 6, 9, and 12 months

* Intermediate analysis to be performed when any out of specification or any significant change observed at Accelerated condition or on demand

Details of stability data available for submission batches

Product	Batch Number	Mfg. Date	Stability Study Start Date	Stability data available upto
Co-amoxiclav Oral Suspension, 200/28.5mg/5ml.	CDCH0003	Jun. 2010	29.06.2010	6 Months accelerated and 36 Months Long term data
	CDCH0004			
Co-amoxiclav Oral Suspension, 400/57mg/5ml.	CDEH0003			
	CDEH0004			

The stability specification and test method utilized for stability studies are provided in **Section 3.2.P.5.1: Specification** and **Section 3.2.P.5.2: Analytical procedures** respectively

The 6 months Accelerated, 18 months Long term including 7 days of reconstitution period stability results complies as per shelf life specifications during stability studies, compiled stability data for the same are provided below in this section.

Accelerated Stability study - Co-amoxiclav 200/28.5mg/5ml Powder for Oral Suspension

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	4.7	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.7	5.0
Water content (By KF)	NMT 10%	7.2 %	8.6 %	7.6 %	8.0 %	9.0 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	99.1 % (198.2 mg)	98.9 % (197.8 mg)	98.2 % (196.4 mg)	96.6 % (193.2 mg)	96.7 % (193.4 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.4 % (196.7 mg)	97.7 % (195.2 mg)	95.7 % (191.3 mg)	97.0 % (194.0 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	109.7 % (31.3 mg)	108.4 % (30.9 mg)	105.7 % (30.0 mg)	102.5 % (29.2 mg)	101.8 % (29.0 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	97.2 % (27.7 mg)	97.5 % (27.8 mg)	95.8 % (27.3 mg)	97.5 % (27.8 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.30 %	0.36 %	0.41 %	0.50 %
	Day 7 - NMT 2.0%	Not applicable	0.41 %	0.33 %	0.39 %	0.46 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.27 %	0.19 %	0.19 %	0.26 %	0.37 %
	Day 7 - NMT 1.0%	Not applicable	0.32 %	0.16 %	0.39 %	0.34 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.10 %	0.10 %	0.07 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.20 %	0.10 %	0.09 %	0.09 %
Total impurities	**Day 0 -** NMT 3.0%	0.88 %	0.65 %	0.75 %	0.97 %	1.11 %
	Day 7 - NMT 3.0%	Not applicable	1.34 %	0.71 %	1.10 %	1.19 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	<10 CFU/g	Not Applicable	Not Applicable	Not Applicable	<10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (3.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.7	4.6	4.5	4.9	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.9	5.1
Water content (By KF)	NMT 10%	7.4 %	8.7 %	7.7 %	7.6 %	7.6 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.7 % (197.3 mg)	99.6 % (199.2 mg)	99.2 % (198.4 mg)	97.9 % (195.8 mg)	96.9 % (193.7 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	99.3 % (198.6 mg)	98.7 % (197.3 mg)	96.0 % (192.0 mg)	96.6 % (193.0 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.4 % (31.5 mg)	109.5 % (31.2 mg)	106.7 % (30.4 mg)	103.9 % (29.6 mg)	102.1 % (29.1 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	101.1 % (28.8 mg)	98.4 % (28.1 mg)	95.0 % (27.1 mg)	94.4 % (26.9 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.36 %	0.37 %	0.38 %	0.48 %
	Day 7 - NMT 2.0%	Not applicable	0.40 %	0.32 %	0.41 %	0.44 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.27 %	0.19 %	0.22 %	0.26 %	0.44 %
	Day 7 - NMT 1.0%	Not applicable	0.39 %	0.17 %	0.38 %	0.33 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.11 %	0.11 %	0.08 %	0.06 %
	Day 7 - NMT 0.5%	Not applicable	0.26 %	0.09 %	0.09 %	0.09 %
Total impurities	**Day 0 -** NMT 3.0%	0.88 %	0.71 %	0.78 %	1.08 %	1.12 %
	Day 7 - NMT 3.0%	Not applicable	1.37 %	0.69 %	1.10 %	1.23 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	<10 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	4.8	5.3
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.8	5.3
Water content (By KF)	NMT 10%	7.3 %	8.6 %	7.5 %	7.7 %	8.8 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.9 % (197.8 mg)	98.9 % (197.0 mg)	97.4 % (194.8 mg)	97.0 % (194.0 mg)	96.9 % (193.7 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.0 % (196.0 mg)	98.0 % (195.9 mg)	95.0 % (189.9 mg)	97.3 % (194.6 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.4 % (31.5 mg)	110.9 % (31.6 mg)	104.9 % (29.9 mg)	101.4 % (28.5 mg)	102.5 % (29.2 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	96.5 % (27.5 mg)	95.8 % (27.3 mg)	96.7 % (27.5 mg)	97.7 % (27.9 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.28 %	0.34 %	0.40 %	0.49 %
	Day 7 - NMT 2.0%	Not applicable	0.35 %	0.30 %	0.39 %	0.43 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.27 %	0.20 %	0.21 %	0.30 %	0.26 %
	Day 7 - NMT 1.0%	Not applicable	0.33 %	0.20 %	0.39 %	0.36 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.12 %	0.07 %	0.07 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.28 %	0.09 %	0.08 %	0.09 %
Total impurities	**Day 0 -** NMT 3.0%	0.88 %	0.66 %	0.67 %	1.07 %	0.98 %
	Day 7 - NMT 3.0%	Not applicable	1.31 %	0.76 %	1.04 %	1.18 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	<10 CFU/g	Not Applicable	Not Applicable	Not Applicable	10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (7.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.6	4.5	4.7	5.3
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.7	5.2
Water content (By KF)	NMT 10%	7.4 %	8.4 %	7.7 %	7.4 %	8.9 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	100.2 % (200.3 mg)	99.5 % (198.9 mg)	98.4 % (196.7 mg)	97.2 % (194.4 mg)	97.4 % (194.8 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	97.7 % (195.4 mg)	97.9 % (195.7 mg)	96.0 % (192.0 mg)	97.6 % (195.2 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	109.8 % (31.3 mg)	109.8 % (31.3 mg)	106.0% (30.2 mg)	101.4 % (28.9 mg)	103.2 % (29.4 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	98.9 % (28.2 mg)	96.8 % (27.6 mg)	96.8 % (27.6 mg)	98.2 % (28.0 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.37 %	0.36 %	0.39 %	0.48 %
	Day 7 - NMT 2.0%	Not applicable	0.36 %	0.33 %	0.35 %	0.41 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.27 %	0.25 %	0.29 %	0.32 %	0.27 %
	Day 7 - NMT 1.0%	Not applicable	0.36 %	0.18 %	0.34 %	0.38 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.09 %	0.07 %	0.08 %	0.08 %
	Day 7 - NMT 0.5%	Not applicable	0.25 %	0.08 %	0.06 %	0.09 %
Total impurities	**Day 0 -** NMT 3.0%	0.88 %	0.79 %	0.79 %	0.96 %	0.97 %
	Day 7 - NMT 3.0%	Not applicable	1.31 %	0.72 %	1.07 %	1.20 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	<10 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (10.0g) sufficient to reconstitute 100ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	4.7	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.6	5.0
Water content (By KF)	NMT 10%	7.4 %	9.2 %	7.8 %	7.8 %	9.2 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.2 % (196.2 mg)	99.6 % (199.2 mg)	99.9 % (199.7 mg)	99.8 % (195.6 mg)	96.7 % (193.4 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.5 % (197.0 mg)	97.7 % (195.4 mg)	96.1 % (192.1 mg)	97.0 % (194.0 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.9 % (31.6 mg)	109.1 % (31.1 mg)	107.7 % (30.7 mg)	103.5 % (29.6 mg)	101.8 % (29.0 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	96.1 % (27.4 mg)	101.0 % (28.8 mg)	97.9 % (27.9 mg)	98.2 % (28.0 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.41 %	0.33 %	0.51 %	0.45 %
	Day 7 - NMT 2.0%	Not applicable	0.49 %	0.32 %	0.52 %	0.40 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.32 %	0.26 %	0.48 %	0.45 %	0.34 %
	Day 7 - NMT 1.0%	Not applicable	0.48 %	0.57 %	0.45 %	0.39 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.14 %	0.14 %	0.14 %	0.10 %
	Day 7 - NMT 0.5%	Not applicable	0.10 %	0.14 %	0.11 %	0.10 %
Total impurities	**Day 0 -** NMT 3.0%	0.95 %	1.17 %	1.35 %	1.36 %	1.12 %
	Day 7 - NMT 3.0%	Not applicable	1.42 %	1.39 %	1.34 %	1.16 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	10 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (3.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.7	4.6	4.6	4.6	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.6	5.0
Water content (By KF)	NMT 10%	7.4	9.0	7.7	7.4	8.3
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	97.9 % (195.8 mg)	99.5 % (199.0 mg)	99.4 % (198.7 mg)	97.7 % (195.3 mg)	99.9 % (199.7 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	97.7 % (195.4 mg)	98.4 % (196.8 mg)	96.4 % (192.7 mg)	98.5 % (197.0 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.7 % (32.1 mg)	107.7 % (30.7 mg)	107.0 % (30.5 mg)	103.9 % (29.6 mg)	104.9 % (29.9 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	96.1 % (27.4 mg)	101.4 % (28.5 mg)	98.2 % (28.0 mg)	99.6 % (28.4 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.40 %	0.39 %	0.55 %	0.43 %
	Day 7 - NMT 2.0%	Not applicable	0.43 %	0.27 %	0.46 %	0.41 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.32 %	0.25 %	0.46 %	0.45 %	0.48 %
	Day 7 - NMT 1.0%	Not applicable	0.64 %	0.53 %	0.49 %	0.37 %
Highest unknown impurity	**Day 0** - NMT 0.5%	0.07 %	0.22 %	0.14 %	0.12 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.09 %	0.12 %	0.11 %	0.10 %
Total impurities	**Day 0** - NMT 3.0%	0.99 %	1.17 %	1.39 %	1.35 %	1.24 %
	Day 7 - NMT 3.0%	Not applicable	1.54 %	1.30 %	1.33 %	1.16 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	<10 CFU/g	Not Applicable	Not Applicable	Not Applicable	10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.5	4.5	4.6	5.3
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.5	4.5	4.6	5.2
Water content (By KF)	NMT 10%	7.4 %	9.2 %	7.3 %	8.4 %	8.3 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.3 % (196.6 mg)	98.4 % (196.8 mg)	98.3 % (196.5 mg)	97.3 % (194.5 mg)	98.7 % (197.3 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	97.0 % (194.0 mg)	97.0 % (194.0 mg)	95.4 % (190.9 mg)	98.1 % (196.2 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.3 % (32.0 mg)	111.9 % (31.9 mg)	107.0 % (30.5 mg)	102.1 % (29.1 mg)	103.2 % (29.4 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	97.9 % (27.9 mg)	99.3 % (28.3 mg)	98.6 % (28.1 mg)	99.3 % (28.3 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.39 %	0.33 %	0.54 %	0.44 %
	Day 7 - NMT 2.0%	Not applicable	0.31 %	0.34 %	0.51 %	0.46 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.32 %	0.26 %	0.28 %	0.50 %	0.35 %
	Day 7 - NMT 1.0%	Not applicable	0.56 %	0.57 %	0.50 %	0.32 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.08 %	0.15 %	0.13 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.10 %	0.09 %	0.11 %	0.10 %
Total impurities	**Day 0 -** NMT 3.0%	0.95 %	0.89 %	1.04 %	1.41 %	1.03 %
	Day 7 - NMT 3.0%	Not applicable	1.40 %	1.24 %	1.36 %	1.10 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (7.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.6	4.5	4.1	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.5	4.5	4.1	5.2
Water content (By KF)	NMT 10%	7.4 %	9.2 %	7.5 %	8.1 %	8.3 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.5 % (196.9 mg)	100.0 % (200.0 mg)	98.9 % (197.8 mg)	97.3 % (194.5 mg)	99.2 % (198.4 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.9 % (197.0 mg)	97.4 % (194.8 mg)	95.8 % (191.6 mg)	98.2 % (196.4 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.5 % (32.1 mg)	108.8 % (31.0 mg)	107.4 % (30.6 mg)	101.4 % (28.9 mg)	103.9 % (29.6 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	98.2 % (28.0 mg)	101.4 % (28.9 mg)	99.0 % (28.2 mg)	99.3 % (28.3 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.38 %	0.32 %	0.51 %	0.44 %
	Day 7 - NMT 2.0%	Not applicable	0.42 %	0.33 %	0.46 %	0.42 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.32 %	0.25 %	0.38 %	0.50 %	0.30 %
	Day 7 - NMT 1.0%	Not applicable	0.47 %	0.43 %	0.50 %	0.35 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.10 %	0.12 %	0.13 %	0.08 %
	Day 7 - NMT 0.5%	Not applicable	0.14 %	0.13 %	0.11 %	0.10 %
Total impurities	**Day 0 -** NMT 3.0%	0.95 %	0.90 %	1.12 %	1.142 %	1.02 %
	Day 7 - NMT 3.0%	Not applicable	1.41 %	1.13 %	1.33 %	1.10 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	30 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (10.0g) sufficient to reconstitute 100ml of solution.

Accelerated Stability study - Co-amoxiclav 400/57mg/5ml Powder for Oral Suspension

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.8	4.6	4.6	4.9	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.7	4.5	4.9	5.1
Water content (By KF)	NMT 10%	7.5 %	8.0 %	6.7 %	7.0 %	8.0 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.7 % (394.7 mg)	99.5 % (398.0 mg)	99.2 % (396.9 mg)	100.1 % (400.2 mg)	100.2 % (400.8 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.0 % (392.0 mg)	98.4 % (393.4 mg)	98.9 % (395.5 mg)	99.0 % (395.8 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.7 % (63.1 mg)	109.3 % (62.3 mg)	111.1 % (63.3 mg)	107.0 % (61.0 mg)	107.2 % (61.1 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	96.7 % (55.1 mg)	96.3 % (54.9 mg)	103.5 % (59.0 mg)	103.5 % (59.0 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.40 %	0.30 %	0.44 %	0.40 %
	Day 7 - NMT 2.0%	Not applicable	0.30 %	0.26 %	0.40 %	0.37 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.28 %	0.29 %	0.35 %	0.27 %	0.28 %
	Day 7 - NMT 1.0%	Not applicable	0.36 %	0.43 %	0.32 %	0.22 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.12 %	0.08 %	0.06 %	0.08 %
	Day 7 - NMT 0.5%	Not applicable	0.19 %	0.09 %	0.06 %	0.07 %
Total impurities	**Day 0 -** NMT 3.0%	0.85 %	0.95 %	1.16 %	0.89 %	1.04 %
	Day 7 - NMT 3.0%	Not applicable	1.30 %	1.15 %	1.02 %	0.94 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	30 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	4.7	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.8	5.1
Water content (By KF)	NMT 10%	7.4 %	8.2 %	6.9 %	7.5 %	7.8 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	99.0 % (395.9 mg)	99.0 % (396.0 mg)	99.0 % (396.1 mg)	99.6 % (398.4 mg)	99.6 % (398.5 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.2 % (388.9 mg)	97.9 % (391.7 mg)	99.6 % (398.4 mg)	99.6 % (398.5 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.2 % (62.3 mg)	110.4 % (62.9 mg)	109.8 % (62.6 mg)	106.7 % (60.8 mg)	106.5 % (60.7 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	96.8 % (55.2 mg)	95.6 % (54.5 mg)	103.5 % (59.0 mg)	104.2 % (59.4 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.34 %	0.35 %	0.45 %	0.40 %
	Day 7 - NMT 2.0%	Not applicable	0.31 %	0.31 %	0.40 %	0.37 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.28 %	0.24%	0.30 %	0.26 %	0.29 %
	Day 7 - NMT 1.0%	Not applicable	0.53 %	0.49 %	0.33 %	0.30 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.11 %	0.09 %	0.07 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.14 %	0.10 %	0.07 %	0.07 %
Total impurities	**Day 0 -** NMT 3.0%	0.85 %	0.81 %	1.13 %	0.92 %	1.10 %
	Day 7 - NMT 3.0%	Not applicable	1.41 %	1.31 %	1.06 %	1.03 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	<10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (12.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.6	4.8	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.9	5.0
Water content (By KF)	NMT 10%	7.4 %	8.1 %	7.0 %	7.3 %	7.7 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	99.8 % (399.0 mg)	99.2 % (396.7 mg)	98.5 % (393.8 mg)	100.5 % (402.0 mg)	100.3 % (401.3 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.7 % (390.7 mg)	97.8 % (391.3 mg)	99.7 % (398.7 mg)	98.8 % (395.8 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.4 % (62.4 mg)	108.9 % (62.1 mg)	105.4 % (60.1 mg)	107.5 % (61.3 mg)	107.2 % (61.1 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	97.5 % (55.6 mg)	95.3 % (54.3 mg)	104.6 % (59.6 mg)	103.3 % (58.9 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.37 %	0.39 %	0.46 %	0.40 %
	Day 7 - NMT 2.0%	Not applicable	0.29 %	0.39 %	0.42 %	0.36 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.28 %	0.31 %	0.48 %	0.31 %	0.32 %
	Day 7 - NMT 1.0%	Not applicable	0.33 %	0.54 %	0.34 %	0.40 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.11 %	0.11 %	0.06 %	0.08 %
	Day 7 - NMT 0.5%	Not applicable	0.27 %	0.22 %	0.07 %	0.06 %
Total impurities	**Day 0 -** NMT 3.0%	0.85 %	1.01 %	1.36 %	0.98 %	1.12 %
	Day 7 - NMT 3.0%	Not applicable	1.34 %	1.60 %	1.04 %	1.13 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (14.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.6	4.7	5.6
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	4.9	5.0
Water content (By KF)	NMT 10%	7.4 %	8.1 %	6.8 %	7.1 %	7.7 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	100.7 % (402.5 mg)	98.5 % (394.0 mg)	97.9 % (391.6 mg)	101.0 % (404.0 mg)	100.3 % (401.3 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.1 % (392.3 mg)	98.4 % (393.6 mg)	99.0 % (395.9 mg)	99.8 % (399.1 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.0 % (62.2 mg)	108.8 % (62.0 mg)	105.1 % (59.5 mg)	107.9 % (61.5 mg)	106.8 % (60.9 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	98.4 % (56.1 mg)	95.6 % (54.5 mg)	103.7 % (59.1 mg)	104.4 % (59.5 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.37 %	0.48 %	0.37 %	0.45 %	0.38 %
	Day 7 - NMT 2.0%	Not applicable	0.18 %	0.37 %	0.48 %	0.38 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.28 %	0.38 %	0.36 %	0.30 %	0.29 %
	Day 7 - NMT 1.0%	Not applicable	0.44 %	0.47 %	0.31 %	0.34 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.07 %	0.19 %	0.08 %	0.06 %	0.08 %
	Day 7 - NMT 0.5%	Not applicable	0.13 %	0.12 %	0.07 %	0.07 %
Total impurities	**Day 0 -** NMT 3.0%	0.85 %	1.38 %	1.13 %	0.92 %	1.10 %
	Day 7 - NMT 3.0%	Not applicable	1.17 %	1.45 %	1.04 %	1.10 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	40 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (20.0g) sufficient to reconstitute 100ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	4.0	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.7	4.5	3.9	5.0
Water content (By KF)	NMT 10%	7.4 %	8.3 %	6.7 %	8.4 %	7.9 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.8 % (395.1 mg)	98.4 % (393.4 mg)	98.7 % (394.9 mg)	100.6 % (402.4 mg)	100.3 % (401.2 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.6 % (390.4 mg)	97.8 % (391.2 mg)	99.0 % (396.1 mg)	99.3 % (397.2 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.1 % (62.8 mg)	109.8 % (62.6 mg)	105.6 % (60.2 mg)	108.6 % (61.9 mg)	106.7 % (60.8 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	94.6 % (53.9 mg)	100.2 % (57.1 mg)	107.5 % (61.3 mg)	104.4 % (59.5 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.39 %	0.31 %	0.37 %	0.43 %
	Day 7 - NMT 2.0%	Not applicable	0.32 %	0.28 %	0.42 %	0.40 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.29 %	0.42 %	0.51 %	0.23 %	0.29 %
	Day 7 - NMT 1.0%	Not applicable	0.60 %	0.58 %	0.35 %	0.28 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.06 %	0.09 %	0.05 %	0.06 %	0.10 %
	Day 7 - NMT 0.5%	Not applicable	0.16 %	0.11 %	0.07 %	0.10 %
Total impurities	**Day 0 -** NMT 3.0%	0.90 %	1.13 %	1.03 %	0.78 %	1.11 %
	Day 7 - NMT 3.0%	Not applicable	1.54 %	1.43 %	0.98 %	1.13 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	20 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	3.9	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	3.9	4.9
Water content (By KF)	NMT 10%	7.4 %	8.3 %	6.6 %	7.8 %	7.4 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.5 % (393.8 mg)	99.2 % (396.8 mg)	99.5 % (398.1 mg)	99.0 % (395.8 mg)	98.7 % (394.6 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.9 % (391.5 mg)	98.0 % (392.1 mg)	98.3 % (393.3 mg)	98.5 % (394.1 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.6 % (62.5 mg)	108.8 % (62.0 mg)	107.4 % (61.2 mg)	106.3 % (60.6 mg)	103.5 % (59.0 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	96.1 % (54.8 mg)	100.7 % (57.4 mg)	104.9 % (59.7 mg)	103.5 % (59.0 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.36 %	0.29 %	0.37 %	0.42 %
	Day 7 - NMT 2.0%	Not applicable	0.30 %	0.29 %	0.45 %	0.40 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.29 %	0.52 %	0.63 %	0.26 %	0.34 %
	Day 7 - NMT 1.0%	Not applicable	0.64 %	0.65 %	0.35 %	0.27 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.06 %	0.10 %	0.09 %	0.06 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.13%	0.21 %	0.18 %	0.07 %
Total impurities	**Day 0 -** NMT 3.0%	0.90 %	1.31 %	1.19 %	0.80 %	1.09 %
	Day 7 - NMT 3.0%	Not applicable	1.60 %	1.48 %	1.13 %	1.15 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	10 CFU/g	Not Applicable	Not Applicable	Not Applicable	30 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (12.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.6	4.0	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.6	3.9	4.9
Water content (By KF)	NMT 10%	7.4 %	8.2 %	7.0 %	8.4 %	7.9 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.5 % (393.8 mg)	99.9 % (399.5 mg)	98.8 % (395.2 mg)	98.1 % (392.4 mg)	99.0 % (396.0 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.5 % (393.9 mg)	97.2 % (388.8 mg)	97.5 % (390.0 mg)	98.4 % (393.4 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.8 % (63.2 mg)	109.3 % (62.3 mg)	106.5 % (60.7 mg)	105.6 % (60.2 mg)	103.9 % (59.2 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	94.7 % (54.0 mg)	99.6 % (56.8 mg)	104.4 % (59.5 mg)	103.2 % (58.8 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.39 %	0.28 %	0.37 %	0.43 %
	Day 7 - NMT 2.0%	Not applicable	0.35 %	0.26 %	0.42 %	0.40 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.29 %	0.56 %	0.66 %	0.28 %	0.33 %
	Day 7 - NMT 1.0%	Not applicable	0.59 %	0.49 %	0.34 %	0.25 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.06 %	0.09 %	0.08 %	0.06 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.11 %	0.12 %	0.06 %	0.08 %
Total impurities	**Day 0 -** NMT 3.0%	0.90 %	1.19 %	1.23 %	0.84 %	1.06 %
	Day 7 - NMT 3.0%	Not applicable	1.73 %	1.22 %	0.96 %	1.14 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	10 CFU/g	Not Applicable	Not Applicable	Not Applicable	10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (14.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 40ºC ± 2ºC & 75% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	1 Month	2 Month	3 Month	6 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.6	4.5	3.9	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.6	4.5	3.9	4.9
Water content (By KF)	NMT 10%	7.4 %	8.1 %	6.6 %	8.4 %	7.5 %
Assay (By HPLC)						
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.2 % (392.6 mg)	98.5 % (393.9 mg)	98.2 % (392.6 mg)	98.2 % (392.6 mg)	100.5 % (402.0 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.9 % (391.5 mg)	94.7 % (378.6 mg)	98.1 % (392.3 mg)	98.5 % (394.1 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	111.8 % (63.7 mg)	107.9 % (61.9 mg)	104.7 % (59.7 mg)	106.2 % (60.5 mg)	103.9 % (59.2 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	97.0 % (55.3 mg)	100.2 % (57.1 mg)	103.0 % (58.7 mg)	103.3 % (58.9 mg)
Related substances (By HPLC)						
Amoxicillin dimer (Impurity -J)	**Day 0 -** NMT 1.5%	0.39 %	0.40 %	0.33 %	0.38 %	0.43 %
	Day 7 - NMT 2.0%	Not applicable	0.45 %	0.25 %	0.41 %	0.40 %
Any individual Known impurity	**Day 0 -** NMT 1.0%	0.29 %	0.59 %	0.58 %	0.27 %	0.32 %
	Day 7 - NMT 1.0%	Not applicable	0.67 %	0.63 %	0.35 %	0.28 %
Highest unknown impurity	**Day 0 -** NMT 0.5%	0.06 %	0.10 %	0.10 %	0.06 %	0.09 %
	Day 7 - NMT 0.5%	Not applicable	0.13 %	0.12 %	0.06 %	0.07 %
Total impurities	**Day 0 -** NMT 3.0%	0.90 %	1.36 %	1.20 %	0.84 %	1.06 %
	Day 7 - NMT 3.0%	Not applicable	1.79 %	1.42 %	0.97 %	1.11 %
Microbiological Quality						
i) Total Bacterial Count	NMT 1000 cfu / g	20 CFU/g	Not Applicable	Not Applicable	Not Applicable	10 CFU/g
ii) Total Fungal Count	NMT 100 cfu / g	<10 CFU/g				<10 CFU/g
iii) Pathogenic Organisms						
Escherichia coli	Should be absent/ g	Absent				Absent

Conclusion The product is stable when stored at Accelerated condition [40ºC ± 2ºC & 75% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (20.0g) sufficient to reconstitute 100ml of solution.

Long Term Stability study - Co-amoxiclav 200/28.5mg/5ml Powder for Oral Suspension

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.7	4.7	4.7	4.9	4.8	4.0	5.8
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.7	4.6	5.2	5.2	4.8	4.0	6.3
Water content (By KF)	NMT 10%	7.2 %	7.2 %	7.6 %	7.4 %	7.6 %	8.0 %	8.5 %	9.5 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	99.1 % (198.2 mg)	101.4 % (202.8 mg)	100.5 % (200.9 mg)	100.8 % (201.7 mg)	99.5 % (199.0 mg)	100.9 % (201.9 mg)	99.8 % (199.6 mg)	100.0 % (200.0 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.7 % (197.4 mg)	100.4 % (200.7 mg)	99.9 % (199.7 mg)	99.1 % (198.2 mg)	100.6 % (201.3 mg)	98.7 % (197.3 mg)	105.0 % (209.9 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	109.7 % (31.3 mg)	110.5 % (31.5 mg)	104.2 % (29.7 mg)	106.3 % (30.3 mg)	109.0 % (31.1 mg)	108.0 % (30.8 mg)	105.3 % (30.0 mg)	99.5 % (28.37 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	99.7 % (28.4 mg)	100.0 % (28.5 mg)	101.8 % (29.0 mg)	99.2 % (28.3 mg)	96.8 % (27.6 mg)	98.4 % (28.0 mg)	92.2 % (26.27 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.41 %	0.44 %	0.49 %	0.48 %	0.51 %	0.36 %	0.41 %
	Day 7 - NMT 2.0%	Not applicable	0.36 %	0.47 %	0.52 %	0.46 %	0.39 %	0.36 %	0.43 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.27 %	0.26 %	0.28 %	0.22 %	0.24 %	0.25 %	0.15 %	0.25 %
	Day 7 - NMT 1.0%	Not applicable	0.34 %	0.30 %	0.24 %	0.40 %	0.21 %	0.14 %	0.34 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.08 %	0.08 %	0.36 %	0.11 %	Not detected	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.14 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.17 %	0.09 %	0.15 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.06 %	0.10 %
Total impurities	**Day 0** - NMT 3.0%	0.88 %	0.86 %	0.96 %	1.64 %	1.14 %	0.96 %	0.65 %	1.30 %
	Day 7 - NMT 3.0%	Not applicable	0.97 %	1.10 %	1.31 %	1.28 %	1.28 %	0.75 %	1.55 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	<10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (3.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.7	4.9	4.7	4.7	5.0	4.8	4.1	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.8	4.6	5.6	5.2	4.7	4.1	6.1
Water content (By KF)	NMT 10%	7.4 %	7.2 %	7.6 %	7.6 %	7.3 %	7.7 %	7.9 %	8.6 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.7 % (197.3 mg)	100.3 % (200.5 mg)	101.4 % (202.8 mg)	101.0 % (201.9 mg)	99.9 % (199.8 mg)	100.6 % (201.2 mg)	100.5 % (201.1 mg)	101.4 % (202.8 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	99.1 % (198.1 mg)	100.2 % (200.4 mg)	99.0 % (198.1 mg)	99.7 % (199.4 mg)	100.8 % (201.5 mg)	98.6 % (197.1 mg)	97.9 % (195.8)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.4 % (31.5 mg)	108.8 % (31.0 mg)	104.9 % (29.9 mg)	109.4 % (31.2 mg)	109.2 % (31.1 mg)	105.3 % (30.0 mg)	105.1 % (30.0 mg)	107.4 % (30.62 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	100.0 % (28.5 mg)	99.6 % (28.4 mg)	101.2 % (28.8 mg)	99.7 % (28.4 mg)	96.8 % (27.6 mg)	98.2 % (28.0 m7)	98.1 % (27.96 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.38 %	0.46 %	0.45 %	0.48 %	0.53 %	0.36 %	0.39 %
	Day 7 - NMT 2.0%	Not applicable	0.33 %	0.46 %	0.50 %	0.43 %	0.40 %	0.36 %	0.38 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.27 %	0.25 %	0.30 %	0.20 %	0.23 %	0.22 %	0.17 %	0.20 %
	Day 7 - NMT 1.0%	Not applicable	0.44 %	0.31 %	0.24 %	0.36 %	0.25 %	0.16 %	0.21 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.08 %	0.09 %	0.35 %	0.09 %	0.05 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.11 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.17 %	0.08 %	0.07 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.09 %
Total impurities	**Day 0** - NMT 3.0%	0.88 %	0.83 %	1.02 %	1.64 %	1.05 %	1.05 %	0.78 %	0.96 %
	Day 7 - NMT 3.0%	Not applicable	1.05 %	1.10 %	1.18 %	1.16 %	0.98 %	0.83 %	1.27 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	<10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.9	4.7	4.6	5.0	4.8	4.1	5.0
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.9	4.7	5.1	5.2	4.8	4.1	6.1
Water content (By KF)	NMT 10%	7.3 %	7.6 %	7.3 %	7.4 %	7.2 %	7.6 %	9.8 %	8.4 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.9 % (197.8 mg)	99.1 % (198.1 mg)	100.3 % (201.3 mg)	101.2 % (202.3 mg)	100.5 % (200.9 mg)	102.2 % (204.5 mg)	100.4 % (200.8 mg)	102.3 % (204.6)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	97.7 % (195.4 mg)	101.2 % (202.3 mg)	99.1 % (198.2 mg)	99.3 % (198.6 mg)	101.0 % (202.0 mg)	98.5 % (197.0 mg)	98.7 % 197.3
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.4 % (31.5 mg)	107.8 % (30.7 mg)	104.2 % (29.7 mg)	108.6 % (30.9 mg)	108.4 % (30.9 mg)	106.5 % (30.3 mg)	104.2 % (29.7 mg)	109.2 % (31.12)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	99.3 % (28.3 mg)	100.7 % (28.7 mg)	101.0 % (28.8 mg)	99.3 % (28.3 mg)	97.2 % (27.7 mg)	97.6 % (27.8 mg)	100.0 % (28.51)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.39 %	0.45 %	0.48 %	0.49 %	0.51 %	0.37 %	0.44 %
	Day 7 - NMT 2.0%	Not applicable	0.36 %	0.44 %	0.48 %	0.44 %	0.35 %	0.37 %	0.41 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.27 %	0.28 %	0.35 %	0.23 %	0.23 %	0.22 %	0.17 %	0.22 %
	Day 7 - NMT 1.0%	Not applicable	0.33 %	0.35 %	0.29 %	0.37 %	0.20 %	0.18 %	0.20 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.08 %	0.08 %	0.33 %	0.09 %	0.06 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.12 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.18 %	0.08 %	0.09 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.11 %	0.09 %
Total impurities	**Day 0** - NMT 3.0%	0.88 %	0.86 %	1.04 %	1.70 %	1.11 %	0.99 %	0.86 %	1.12 %
	Day 7 - NMT 3.0%	Not applicable	0.95 %	1.12 %	1.15 %	1.26 %	1.07 %	0.82 %	1.25 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	<10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (7.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.9	4.7	4.7	5.0	4.8	4.1	5.0
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.9	4.7	5.4	5.1	4.7	4.0	6.0
Water content (By KF)	NMT 10%	7.4 %	7.6 %	7.4 %	7.4 %	7.3 %	7.6 %	7.7 %	8.5 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	100.2 % (200.3 mg)	99.1 % (198.1 mg)	102.7 % (205.3 mg)	101.0 % (202.0 mg)	100.1 % (200.2 mg)	101.4 % (202.8 mg)	100.1 % (200.2 mg)	98.2 % (196.3 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	97.9 % (195.7 mg)	102.5 % (205.0 mg)	100.1 % (200.1 mg)	98.6 % (197.2 mg)	100.9 % (201.8 mg)	98.5 % (197.1 mg)	98.9 % (197.8 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	109.8 % (31.3 mg)	107.4 % (30.6 mg)	106.3 % (30.3 mg)	108.7 % (31.0 mg)	109.0 % (31.1 mg)	105.8 % (30.1 mg)	102.6 % (29.23 mg)	110.8 % (31.58 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	99.7 % (28.4 mg)	102.5 % (29.2 mg)	101.8 % (29.0 mg)	98.3 % (28.0 mg)	97.1 % (27.7 mg)	97.6 % (27.81 mg)	94.81 % (27.02 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.36 %	0.46 %	0.45 %	0.50 %	0.50 %	0.38 %	0.43 %
	Day 7 - NMT 2.0%	Not applicable	0.36 %	0.44 %	0.45 %	0.48 %	0.38 %	0.36 %	0.40 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.27 %	0.28 %	0.34 %	0.20 %	0.22 %	0.20 %	0.20 %	0.21 %
	Day 7 - NMT 1.0%	Not applicable	0.50 %	0.34 %	0.25 %	0.37 %	0.18 %	0.19 %	0.19 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.09 %	0.08 %	0.30 %	0.10 %	0.06 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.09 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.08 %	0.20 %	0.08 %	0.07 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.88 %	0.88 %	1.03 %	1.65 %	1.06 %	1.05 %	0.74 %	1.02 %
	Day 7 - NMT 3.0%	Not applicable	1.20 %	1.09 %	1.20 %	1.27 %	1.06 %	0.78 %	1.08 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	<10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (10.0g) sufficient to reconstitute 100ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.0	4.7	4.7	5.0	4.8	4.2	5.8
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.0	4.6	5.3	5.2	4.8	4.1	6.4
Water content (By KF)	NMT 10%	7.4 %	8.3 %	7.6 %	7.7 %	6.9 %	8.1 %	8.7 %	9.5 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.2 % (196.2 mg)	99.8 % (199.5 mg)	100.1 % (200.1 mg)	101.1 % (202.2 mg)	100.0 % (200.0 mg)	101. % (201.9 mg)	100.0 % (200.1 mg)	99.9 % (199.8 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	99.5 % (198.5 mg)	99.1 % (198.1 mg)	100.5 % (201.0 mg)	98.5 % (197.1 mg)	100.7 % (201.4 %)	98.6 % (197.1 mg)	104.0 % (208.0 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	110.9 % (31.6 mg)	108.4 % (30.9 mg)	101.1 % (28.8 mg)	109.0 % (31.1 mg)	109.1 % (31.1 mg)	107.8 % (30.72 mg)	102.8 % (29.31 mg)	99.8 % (28.46 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	101.4 % (28.5 mg)	99.3 % (28.3 mg)	101.5 % (28.9 mg)	98.2 % (28.0 mg)	96.8 % (27.59 mg)	97.3 % (27.73 mg)	92.6 % (26.40 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.42 %	0.43 %	0.37 %	0.45 %	0.41 %	0.36 %	0.34 %
	Day 7 - NMT 2.0%	Not applicable	0.37 %	0.40 %	0.28 %	0.44 %	0.35 %	0.30 %	0.29 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.32 %	0.38 %	0.26 %	0.22 %	0.23 %	0.20 %	0.15 %	0.22 %
	Day 7 - NMT 1.0%	Not applicable	0.38 %	0.29 %	0.21 %	0.37 %	0.29 %	0.15 %	0.25 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.09 %	0.09 %	0.24 %	0.10 %	0.16 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.12 %	0.14 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.10 %	0.07 %	0.17 %	0.07 %	0.13 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.08 %	0.19 %
Total impurities	**Day 0** - NMT 3.0%	0.95 %	1.05 %	0.96 %	1.34 %	1.12 %	1.02 %	0.86 %	1.09 %
	Day 7 - NMT 3.0%	Not applicable	1.06 %	0.98 %	0.93 %	1.27 %	0.96 %	0.80 %	1.41 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						< 10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (3.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.7	3.9	4.7	4.6	4.9	4.8	4.1	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	3.8	4.7	5.3	5.2	4.8	4.1	6.2
Water content (By KF)	NMT 10%	7.4 %	7.5 %	7.5 %	7.5 %	7.6 %	7.8 %	8.1 %	9.0 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	97.9 % (195.8 mg)	100.3 % (200.5 mg)	99.7 % (199.4 mg)	101.6 % (203.1 mg)	100.4 % (200.7 mg)	100.1 % (200.1 mg)	100.7 % (201.5 mg)	97.4 % (194.9 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.8 % (197.5 mg)	99.3 % (198.5 mg)	103.6 % (207.2 mg)	98.7 % (197.3 mg)	100.7 % (201.4 mg)	98.8 % (197.6)	93.1 % (186.1 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.7 % (32.1 mg)	107.3 % (30.7 mg)	101.1 % (28.8 mg)	109.5 % (31.2 mg)	109.8 % (31.3 mg)	104.3 % (29.74 mg)	103.2 % (29.41 mg)	108.4 % (30.91 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	100.7 % (28.7 mg)	99.3 % (28.3 mg)	104.6 % (29.8 mg)	98.4 % (28.1 mg)	96.3 % (27.44 mg)	97.6 % (27.82 mg)	113.9 % (32.45 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.39 %	0.44 %	0.42 %	0.42 %	0.40 %	0.36 %	0.35 %
	Day 7 - NMT 2.0%	Not applicable	0.37 %	0.41 %	0.31 %	0.46 %	0.32 %	0.31 %	0.31 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.32 %	0.38 %	0.27 %	0.25 %	0.26 %	0.21 %	0.16 %	0.19 %
	Day 7 - NMT 1.0%	Not applicable	0.33 %	0.32 %	0.17 %	0.37 %	0.24 %	0.14 %	0.25 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.07 %	0.09 %	0.22 %	0.08 %	0.17 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.09 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.10 %	0.09 %	0.15 %	0.09 %	0.11 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.09 %
Total impurities	**Day 0** - NMT 3.0%	0.99 %	1.03 %	0.97 %	1.44 %	0.95 %	0.99 %	0.76 %	0.91 %
	Day 7 - NMT 3.0%	Not applicable	1.02 %	1.04 %	0.98 %	1.29 %	0.82 %	0.70 %	1.12 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	<10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.0	4.7	4.6	5.1	4.7	4.2	5.0
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	3.9	4.7	5.8	5.1	4.7	4.1	6.1
Water content (By KF)	NMT 10%	7.4 %	7.8 %	7.6 %	7.4 %	8.1 %	8.7 %	10.0 %	8.4 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.3 % (196.6 mg)	99.6 % (199.2 mg)	100.4 % (200.8 mg)	100.2 % (200.3 mg)	99.6 % (199.2 mg)	101.6 % (203.2 mg)	100.0 % (200.0 mg)	99.0 % (197.9 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.6 % (197.1 mg)	99.7 % (199.3 mg)	99.7 % (199.3 mg)	99.0 % (198.0 mg)	100.8 % (201.6 mg)	98.7 % (197.4 mg)	94.3 % (188.5 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.3 % (32.0 mg)	108.8 % (31.0 mg)	101.8 % (29.0 mg)	108.7 % (31.0 mg)	107.7 % (30.7 mg)	105.7 % (30.13 mg)	103.1 % (29.39 mg)	106.5 % (30.34 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	100.0 % (28.5 mg)	99.6 % (28.4 mg)	100.6 % (28.7 mg)	98.7 % (28.1 mg)	96.5 % (27.50 mg)	97.5 % (27.78 mg)	105.3 % (30.02 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.44 %	0.43 %	0.40 %	0.42 %	0.42 %	0.37 %	0.36 %
	Day 7 - NMT 2.0%	Not applicable	0.38 %	0.37 %	0.32 %	0.42 %	0.33 %	0.31 %	0.32 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.32 %	0.39 %	0.26 %	0.23 %	0.23 %	0.18 %	0.18 %	0.20 %
	Day 7 - NMT 1.0%	Not applicable	0.35 %	0.32 %	0.34 %	0.26 %	0.24 %	0.18 %	0.20 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.07 %	0.09 %	0.21 %	0.15 %	0.20 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.09 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.13 %	0.10 %	0.10 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.08 %
Total impurities	**Day 0** - NMT 3.0%	0.95 %	1.05 %	0.95 %	1.32 %	1.13 %	1.00 %	0.80 %	0.93 %
	Day 7 - NMT 3.0%	Not applicable	1.03 %	1.00 %	1.18 %	1.16 %	0.78 %	0.79 %	1.03 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (7.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDCH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	5.0	4.0	4.7	4.6	5.0	4.8	4.1	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.0	4.7	5.7	5.2	4.7	4.0	6.1
Water content (By KF)	NMT 10%	7.4 %	8.0 %	7.7 %	7.6 %	9.1 %	7.4 %	7.9 %	8.6 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 190.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	98.5 % (196.9 mg)	99.1 % (198.2 mg)	101.0 % (201.9 mg)	100.5 % (201.1 mg)	99.7 % (199.4 mg)	101.6 % (203.2 mg)	100.1 % (200.3 mg)	100.0 % (200.0 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 184.0 mg and NMT 210.0 mg Amoxicillin per 5 ml)	Not applicable	98.4 % (196.7 mg)	99.4 % (198.8 mg)	99.7 % (199.5 mg)	99.3 % (198.6 mg)	100.7 % (201.3 mg)	98.5 % (197.0 mg)	103.5 % (206.9 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 27.07 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	112.5 % (32.1 mg)	107.0 % (30.5 mg)	102.1 % (29.1 mg)	108.8 % (30.4 mg)	107.8 % (30.73 mg)	105.5 % (30.07 mg)	103.2 % (29.41 mg)	105.3 % (30.02 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 26.21 mg and NMT 32.77 mg of Clavulanic acid per 5 ml)	Not applicable	99.7 % (28.4 mg)	99.3 % (28.3 mg)	100.2 % (28.6 mg)	98.9 % (28.2 mg)	96.4 % (27.47 mg)	97.3 % (27.72 mg)	102.9 % (29.34 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.41 %	0.42 %	0.43 %	0.45 %	0.42 %	0.37 %	0.35 %
	Day 7 - NMT 2.0%	Not applicable	0.37 %	0.38 %	0.30 %	0.43 %	0.35 %	0.32 %	0.31 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.32 %	0.43 %	0.30 %	0.28 %	0.25 %	0.15 %	0.20 %	0.19 %
	Day 7 - NMT 1.0%	Not applicable	0.37 %	0.34 %	0.26 %	0.36 %	0.27 %	0.21 %	0.19 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.07 %	0.09 %	0.19 %	0.23 %	0.19 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.09 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.10 %	0.09 %	0.11 %	0.09 %	0.09 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.14 %	0.09 %
Total impurities	**Day 0** - NMT 3.0%	0.95 %	1.09 %	0.98 %	1.38 %	1.29 %	1.05 %	0.81 %	0.90 %
	Day 7 - NMT 3.0%	Not applicable	1.05 %	1.03 %	0.88 %	1.13 %	0.83 %	0.95 %	1.07 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	30CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (10.0g) sufficient to reconstitute 100ml of solution.

Long Term Stability study - Co-amoxiclav 400/57mg/5ml Powder for Oral Suspension

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.8	4.8	4.8	4.7	5.6	4.7	4.1	5.3
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.9	6.2	5.2	5.6	4.8	4.0	6.2
Water content (By KF)	NMT 10%	7.5 %	7.1 %	7.4 %	8.4 %	7.7 %	7.4 %	7.8 %	8.5 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.7 % (394.7 mg)	99.5 % (398.1 mg)	97.3 % (389.1 mg)	100.0 % (399.9 mg)	99.8 % (399.3 mg)	100.2 % (400.8 mg)	99.9 % (399.6 mg)	99.2 % (396.6 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	99.4 % (397.7 mg)	96.5 % (386.1 mg)	98.8 % (395.3 mg)	98.7 % (394.9 mg)	99.2 % (397.0 mg)	98.8 % (395.1 mg)	98.5 % (393.9 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.7 % (63.1 mg)	106.5 % (60.7 mg)	107.9 % (61.5 mg)	106.7 % (60.8 mg)	104.8 % (59.8 mg)	104.3 % (59.5 mg)	102.9 % (58.6 mg)	103.7 % (59.12 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	102.8 % (58.6 mg)	99.1 % (56.5 mg)	104.3 % (59.5 mg)	103.7 % (59.1 mg)	102.6 % (58.5 mg)	97.4 % (55.5 mg)	94.9 % (54.07 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.42 %	0.41 %	0.49 %	0.51 %	0.56 %	0.35 %	0.45 %
	Day 7 - NMT 2.0%	Not applicable	0.41 %	0.36 %	0.39 %	0.35 %	0.39 %	0.26 %	0.29 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.28 %	0.23 %	0.26 %	0.24 %	0.25 %	0.24 %	0.19 %	0.45 %
	Day 7 - NMT 1.0%	Not applicable	0.29 %	0.27 %	0.24 %	0.24 %	0.25 %	0.09 %	0.29 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.06 %	0.07 %	0.06 %	0.08 %	0.08 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.08 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.07 %	0.08 %	0.08 %	0.09 %	0.13 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.13 %
Total impurities	**Day 0** - NMT 3.0%	0.85 %	0.84 %	0.90 %	0.96 %	0.96 %	1.12 %	0.77 %	1.03 %
	Day 7 - NMT 3.0%	Not applicable	0.99 %	0.92 %	0.96 %	0.91 %	1.16 %	0.57 %	1.28 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.7	4.7	4.7	5.1	4.8	4.1	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.8	6.3	5.3	5.1	4.8	4.0	5.9
Water content (By KF)	NMT 10%	7.4 %	7.7 %	7.5 %	7.5 %	7.9 %	6.8 %	7.7 %	7.8 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	99.0 % (395.9 mg)	99.8 % (398.9 mg)	96.2 % (384.7 mg)	99.4 % (397.5 mg)	99.3 % (397.1 mg)	99.3 % (397.2 %)	100.1 % (400.3 mg)	99.2 % (396.6 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	99.7 % (398.6 mg)	96.3 % (385.0 mg)	99.5 % (397.9 mg)	103.5 % (394.6 mg)	98.5 % (394.1 %)	98.8 % (395.3 mg)	98.1 % (392.5 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.2 % (62.3 mg)	106.9 % (60.9 mg)	107.0 % (61.0 mg)	106.0 % (60.4 mg)	104.2 % (59.4 mg)	103.7 % (59.1 mg)	103.0 % (58.7 mg)	103.5 % (59.02 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	102.8 % (58.6 mg)	99.1 % (56.5 mg)	104.9 % (59.8 mg)	103.5 % (59.0 mg)	101.5 % (57.8 mg)	97.3 % (55.5 mg)	94.5 % (53.85 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.43 %	0.40 %	0.48 %	0.45 %	0.52 %	0.36 %	0.41 %
	Day 7 - NMT 2.0%	Not applicable	0.40 %	0.37 %	0.40 %	0.36 %	0.39 %	0.26 %	0.28 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.28 %	0.25 %	0.28 %	0.24 %	0.24 %	0.25 %	0.20 %	0.41 %
	Day 7 - NMT 1.0%	Not applicable	0.34 %	0.29 %	0.23 %	0.23 %	0.26 %	0.11 %	0.28 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.06 %	0.07 %	0.06 %	0.14 %	0.10 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.08 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.07 %	0.07 %	0.08 %	0.08 %	0.17 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.06 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.85 %	0.86 %	0.90 %	0.95 %	1.16 %	1.16 %	0.77 %	0.89 %
	Day 7 - NMT 3.0%	Not applicable	1.06 %	0.96 %	0.90 %	0.91 %	1.19 %	0.59 %	0.90 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (12.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.8	4.8	4.7	5.1	4.8	4.1	5.0
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	5.0	6.2	5.7	5.0	4.8	4.1	5.9
Water content (By KF)	NMT 10%	7.4 %	7.6 %	7.6 %	7.5 %	7.7 %	7.6 %	7.2 %	8.4 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	99.8 % (399.0 mg)	99.2 % (396.7 mg)	97.1 % (388.4 mg)	99.8 % (399.2 mg)	99.4 % (397.6 mg)	99.0 % (396.0 mg)	99.9 % (399.4 mg)	99.3 % (397.0 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.8 % (394.2 mg)	97.2 % (388.9 mg)	100.1 % (400.3 mg)	98.7 % (395.0 mg)	97.8 % (391.4 mg)	98.7 % (394.8 mg)	97.6 % (390.2 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.4 % (62.4 mg)	105.9 % (60.4 mg)	107.9 % (61.5 mg)	106.6 % (60.8 mg)	104.4 % (59.5 mg)	103.4 % (59.0 mg)	103.3 % (58.9 mg)	103.6 % (59.08 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	101.8 % (58.0 mg)	99.8 % (56.9 mg)	97.6 % (55.7 mg)	103.5 % (59.0 mg)	100.8 % (57.4 mg)	97.5 % (55.6 mg)	93.9 % (53.50 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.42 %	0.41 %	0.44 %	0.41 %	0.47 %	0.36 %	0.34 %
	Day 7 - NMT 2.0%	Not applicable	0.39 %	0.38 %	0.34 %	0.39 %	0.41 %	0.26 %	0.23 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.28 %	0.25 %	0.28 %	0.23 %	0.15 %	0.22 %	0.22 %	0.34 %
	Day 7 - NMT 1.0%	Not applicable	0.18 %	0.33 %	0.28 %	0.21 %	0.27 %	0.12 %	0.23 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.06 %	0.07 %	0.06 %	0.12 %	0.14 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.08 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.07 %	0.08 %	0.08 %	0.07 %	0.12 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						Not detected	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.85 %	0.84 %	0.93 %	0.89 %	0.83 %	1.15 %	0.79 %	0.68 %
	Day 7 - NMT 3.0%	Not applicable	1.08 %	1.00 %	0.95 %	0.83 %	1.13 %	0.48 %	0.86 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (14.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0003	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.8	4.9	4.7	5.1	5.1	4.0	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.9	6.3	5.3	5.0	4.8	4.0	6.2
Water content (By KF)	NMT 10%	7.4 %	7.1 %	7.8 %	7.7 %	7.5 %	7.6 %	7.6 %	8.1 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	100.7 % (402.5 mg)	99.1 % (396.7 mg)	96.5 % (385.8 mg)	100.7 % (402.8 mg)	99.8 % (399.4 mg)	99.5 % (398.1 mg)	99.7 % (398.8 mg)	99.6 % (397.4 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.8 % (395.0 mg)	96.3 % (385.2 mg)	99.2 % (396.8 mg)	99.0 % (396.1 mg)	98.9 % (395.5 mg)	98.5 % (394.1 mg)	98.1 % (392.3 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.0 % (62.2 mg)	106.0 % (60.4 mg)	107.1 % (61.1 mg)	107.4 % (61.2 mg)	104.8 % (59.8 mg)	103.6 % (59.1 mg)	102.9 % (58.7 mg)	103.8 % (59.16 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	101.6 % (57.9 mg)	98.8 % (56.3 mg)	104.6 % (59.6 mg)	103.7 % (59.1 mg)	101.6 % (57.9 mg)	97.1 % (55.4 mg)	94.4 % (53.80 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.37 %	0.42 %	0.42 %	0.46 %	0.46 %	0.49 %	0.36 %	0.41 %
	Day 7 - NMT 2.0%	Not applicable	0.40 %	0.36 %	0.35 %	0.40 %	0.42 %	0.26 %	0.28 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.28 %	0.27 %	0.32 %	0.26 %	0.18 %	0.18 %	0.21 %	0.41 %
	Day 7 - NMT 1.0%	Not applicable	0.29 %	0.31 %	0.33 %	0.23 %	0.28 %	0.14 %	0.28 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.07 %	0.06 %	0.08 %	0.06 %	0.13 %	0.16 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.08 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.07 %	0.09 %	0.09 %	0.06 %	0.12 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.06 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.85 %	0.86 %	0.99 %	1.01 %	0.88 %	1.26 %	0.78 %	0.83 %
	Day 7 - NMT 3.0%	Not applicable	1.03 %	0.97 %	1.05 %	0.72 %	1.24 %	0.65 %	0.89 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (20.0g) sufficient to reconstitute 100ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 30 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.0	4.8	4.9	5.1	4.8	4.1	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	3.9	6.2	5.6	5.0	4.7	4.0	6.0
Water content (By KF)	NMT 10%	7.4 %	7.2 %	7.6 %	7.7 %	7.8 %	10.0 %	8.4 %	8.9 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.8 % (395.1 mg)	99.4 % (397.5 mg)	96.3% (385.1 mg)	99.8 % (399.0 mg)	99.6 % (398.5 mg)	99.3 % (397.1 mg)	99.5 % (398.1 mg)	99.4 % (397.7 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.2 % (392.9 mg)	96.3 % (385.3 mg)	95.1 % (380.0 mg)	98.6 % (394.4 mg)	98.7 % (394.8 mg)	98.5 % (394.0 mg)	97.9 % (391.5 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.1 % (62.8 mg)	105.1 % (59.9 mg)	106.8 % (60.9 mg)	106.1 % (60.5 mg)	104.2 % (59.4 mg)	103.8 % (59.2 mg)	102.6 % (58.51 mg)	103.9 % (59.22 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	103.9 % (59.2 mg)	98.1 % (55.9 mg)	99.7 % (56.8 mg)	102.8 % (58.6 mg)	101.3 % (57.7 mg)	97.2 % (55.4 mg)	94.2 % (53.70 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.36 %	0.37 %	0.46 %	0.32 %	0.48 %	0.32 %	0.35 %
	Day 7 - NMT 2.0%	Not applicable	0.38 %	0.39 %	0.40 %	0.37 %	0.33 %	0.27 %	0.28 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.29 %	0.30 %	0.40 %	0.24 %	0.14 %	0.30 %	0.07 %	0.35 %
	Day 7 - NMT 1.0%	Not applicable	0.32 %	0.30 %	0.38 %	0.27 %	0.33 %	0.16 %	0.28 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.06 %	0.06 %	0.07 %	0.08 %	0.08 %	0.17 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.06 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.07 %	0.18 %	0.09 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.06 %
Total impurities	**Day 0** - NMT 3.0%	0.90 %	0.88 %	1.00 %	0.94 %	0.58 %	1.34 %	0.52 %	0.78 %
	Day 7 - NMT 3.0%	Not applicable	0.92 %	1.00 %	1.06 %	1.33 %	1.14 %	0.67 %	0.83 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

60 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (6.0g) sufficient to reconstitute 30ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 60 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	3.9	4.7	4.8	4.9	4.8	4.2	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	3.9	6.2	5.9	5.8	4.8	4.1	6.0
Water content (By KF)	NMT 10%	7.4 %	7.3 %	7.6 %	7.5 %	7.5 %	7.5 %	7.5 %	10 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.5 % (393.8 mg)	98.1 % (392.2 mg)	95.9 % (383.5 mg)	98.9 % (395.5 mg)	99.6 % (398.3 mg)	99.9 % (399.6 mg)	99.6 % (398.4 mg)	99.2 % (396.8 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	97.0 % (388.0 mg)	96.3 % (385.1 mg)	98.4 % (393.7 mg)	98.7 % (395.0 mg)	98.8 % (395.1 mg)	98.6 v (394.3 mg)	98.5 % (394.1 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	109.6 % (62.5 mg)	105.1 % (59.9 mg)	106.1 % (60.5 mg)	105.9 % (60.4 mg)	104.1 % (59.4 mg)	104.2 % (59.4 mg)	102.6 % (58.5 mg)	103.8 % (59.15 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	104.4 % (59.5 mg)	97.4 % (55.5 mg)	102.4 % (58.4 mg)	103.0 % (58.7 mg)	101.5 % (57.8 mg)	97.1 % (55.4 mg)	94.8 % (54.01 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.36 %	0.39 %	0.40 %	0.33 %	0.44 %	0.33 %	0.33 %
	Day 7 - NMT 2.0%	Not applicable	0.38 %	0.35 %	0.38 %	0.33 %	0.30 %	0.27 %	0.24 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.29 %	0.29 %	0.27 %	0.23 %	0.19 %	0.20 %	0.12 %	0.33 %
	Day 7 - NMT 1.0%	Not applicable	0.32 %	0.32 %	0.27 %	0.27 %	0.33 %	0.17 %	0.24 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.06 %	0.06 %	0.07 %	0.11 %	Not detected	0.16 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.13 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.10 %	0.07 %	0.17 %	0.09 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.06 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.90 %	0.87 %	0.89 %	0.91 %	0.55 %	1.16 %	0.71 %	0.65 %
	Day 7 - NMT 3.0%	Not applicable	0.91 %	0.97 %	0.96 %	1.18 %	1.22 %	0.66 %	0.73 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (12.0g) sufficient to reconstitute 60ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 70 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.0	4.7	4.7	5.1	4.8	4.1	5.2
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	3.9	6.2	5.8	4.9	4.8	4.0	6.1
Water content (By KF)	NMT 10%	7.4 %	8.4 %	6.9 %	7.6 %	7.5 %	7.2 %	7.7 %	7.9 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.5 % (393.8 mg)	100.9 % (403.7 mg)	96.3 % (385.2 mg)	99.7 % (398.6 mg)	99.3 % (397.3 mg)	99.2 % (396.7 mg)	99.8 % (399.1 mg)	99.6 % (398.4 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	98.1 % (392.5 mg)	96.7 % (386.8 mg)	97.4 % (389.5 mg)	98.7 % (394.9 mg)	98.5 % (393.9 mg)	98.7 % (394.9 mg)	98.4 % (393.4 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	110.8 % (63.2 mg)	108.9 % (62.1 mg)	107.0 % (61.0 mg)	105.8 % (60.3 mg)	103.8 % (59.2 mg)	103.1 % (58.7 mg)	102.7 % (58.54 mg)	104.7 % (59.67 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	106.0 % (60.4 mg)	99.8 % (56.9 mg)	102.4 % (58.4 mg)	103.0 % (58.7 mg)	101.0 % (57.6 mg)	97.1 % (55.3 mg)	94.6 % (53.94 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.36 %	0.40 %	0.38 %	0.44 %	0.48 %	0.28 %	0.41 %
	Day 7 - NMT 2.0%	Not applicable	0.40 %	0.35 %	0.40 %	0.36 %	0.30 %	0.27 %	0.27 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.29 %	0.33 %	0.32 %	0.22 %	0.18 %	0.25 %	0.10 %	0.41 %
	Day 7 - NMT 1.0%	Not applicable	0.35 %	0.31 %	0.27 %	0.19 %	0.38 %	0.20 %	0.27 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.06 %	0.05 %	0.07 %	0.08 %	0.07 %	0.14 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.13 %	0.07 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.10 %	0.08 %	0.07 %	0.22 %	0.14 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.90 %	0.93 %	0.96 %	0.83 %	0.71 %	1.24 %	0.64 %	0.82 %
	Day 7 - NMT 3.0%	Not applicable	1.02 %	0.94 %	0.93 %	1.23 %	1.43 %	0.74 %	0.86 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	10CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].

115 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (14.0g) sufficient to reconstitute 70ml of solution.

MICRO LABS LTD
COMMON TECHNICAL DOCUMENT MODULE 3, QUALITY
CO-AMOXICLAV 200/28.5mg/5ml, 400/57mg/5ml POWDER FOR ORAL SUSPENSION

Batch Number	: CDEH0004	**Date of commencement**	: 29-06-2010	**Batch Size**	: 90.0 Kg
Mfg. Date	: June 2010	**API Source**	: DSM & FERMIC	**Storage Condition**	: 25ºC ± 2ºC & 60% RH ± 5% RH
Exp. Date	: May 2012	**API Batch/Lot No**	: M480840, CKS-2381	**Pack description #**	: 100 ml HDPE container

Test	Specification	0 Month	3 Month	6 Month	9 Month	12 Month	18 Month	24 Month	36 Month
Description (Day 0)	Dry Powder: White to off white powder.	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *	Complies *
	Reconstitution suspension White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
Description (Day 7)	White to off-white suspension with fruity aromatic odour.	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **	Complies **
pH (Day 0)	Should be between 3.8 and 6.6	4.9	4.0	4.8	4.9	5.0	5.1	4.1	5.1
pH (Day 7)	Should be between 3.8 and 6.6	Not applicable	4.0	6.2	5.8	5.0	5.0	4.0	6.3
Water content (By KF)	NMT 10%	7.4 %	7.2 %	7.4 %	7.5 %	7.6 %	7.3 %	7.6 %	8.0 %
Assay (By HPLC)									
Amoxicillin (Day 0)	NLT 95.0% and NMT 105.0% of the label claim. (NLT 380.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	98.2 % (392.6 mg)	100.4 % (401.5 mg)	97.0 % (387.8 mg)	101.2 % (404.9 mg)	99.8 % (399.3 mg)	100.1 % (400.2 mg)	99.6 % (398.4 mg)	99.2 % (396.6 mg)
Amoxicillin (Day 7)	NLT 92.0% and NMT 105.0% of the label claim. (NLT 368.0 mg and NMT 420.0 mg Amoxicillin per 5 ml)	Not applicable	99.2 % (396.8 mg)	97.0 % (387.8 mg)	98.1 % (392.4 mg)	98.6 % (394.3 mg)	99.4 % (397.4 mg)	98.8 % (395.1 mg)	98.2 % (392.6 mg)
Clavulanic acid (Day 0)	NLT 95.0% and NMT 115.0% of the label claim. (NLT 54.15 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	111.8 % (63.7 mg)	108.1 % (61.6 mg)	107.4 % (61.2 mg)	109.5 % (62.4 mg)	104.4 % (59.5 mg)	104.1 % (59.3 mg)	102.5 % (58.4 mg)	103.6 % (59.06 mg)
Clavulanic acid (Day 7)	NLT 92.0% and NMT 115.0% of the label claim. (NLT 52.44 mg and NMT 65.55 mg of Clavulanic acid per 5 ml)	Not applicable	105.6 % (60.2 mg)	97.9 % (55.8 mg)	102.2 % (58.2 mg)	102.7 % (58.6 mg)	102.0 % (58.1 mg)	97.1 % (55.3 mg)	94.4 % (53.80 mg)
Related substances (By HPLC)									
Amoxicillin dimer (Impurity -J)	**Day 0** - NMT 1.5%	0.39 %	0.36 %	0.41 %	0.41 %	0.38 %	0.50 %	0.31 %	0.34 %
	Day 7 - NMT 2.0%	Not applicable	0.39 %	0.38 %	0.36 %	0.35 %	0.32 %	0.27 %	0.26 %
Any individual Known impurity	**Day 0** - NMT 1.0%	0.29 %	0.32 %	0.32 %	0.25 %	0.15 %	0.19 %	0.11 %	0.34 %
	Day 7 - NMT 1.0%	Not applicable	0.39 %	0.31 %	0.26 %	0.25 %	0.37 %	0.21 %	0.26 %
Highest unknown impurity	**Day 0** - NMT 0.5% [Applicable upto 18 months]	0.06 %	0.06 %	0.07 %	0.08 %	Not detected	0.15 %	Not applicable	
	Day 0 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.15 %	0.08 %
	Day 7 - NMT 0.5%[Applicable upto 18 months]	Not applicable	0.09 %	0.09 %	0.07 %	0.27 %	0.16 %	Not applicable	
	Day 7 - NMT 0.2% [Applicable from 24 months]	Not applicable						0.07 %	0.07 %
Total impurities	**Day 0** - NMT 3.0%	0.90 %	0.93 %	0.97 %	0.85 %	0.56 %	1.23 %	0.83 %	0.70 %
	Day 7 - NMT 3.0%	Not applicable	1.32 %	1.00 %	0.90 %	1.34 %	1.35 %	0.70 %	0.93 %
Microbiological Quality									
i) Total Bacterial Count	NMT 1000 cfu / g	20CFU/g	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	<10CFU	<10CFU
ii) Total Fungal Count	NMT 100 cfu / g	<10CFU/g						<10CFU	<10CFU
iii) Pathogenic Organisms									
Escherichia coli	Should be absent/ g	Absent						Absent	Absent

Conclusion The product is stable when stored at Long term condition [25ºC ± 2ºC / 60% RH ± 5% RH].
150 ml HDPE bottle with 28 mm CRC Cap containing off-white dry powder (20.0g) sufficient to reconstitute 100ml of solution.

In the entire stability data, the below expansions are given for symbols.

* White to off white powder.
** White to off-white suspension with fruity aromatic odour
NMT → Not more than
NLT → Not Less than

	MICRO LABS LIMITED, VEERASANDRA
PRODUCT	**Placebo for Co- amoxiclav 400/57mg/5ml Sugar Free Powder For Oral suspension**

Batch Number	: PDAHV0001	Strength	: 400/57 mg/5ml
Mfg. Date	: Jul-14	Exp. Date	: Jun-16
Description of primary Pack	: 115 cc/28mm Heavy Weight HDPE bottle (for 70 ml) with 28 mm CRC Cap with pull tab.		
Source of Primary Pack	: Triveni polymers Pvt Ltd, Mold-Rite Plastics Inc.	Pack Size	: 70ml HDPE
Date of Commencement	: 16/07/14		

Test Intervals		0 month	18 months	24 months	36 months
Specification No.		FPS:R:PDAHV:EU01			
Tests	**Specification Limits**				
Initial analysis					
Description i) Dry powder ii) Reconstituted suspension	 White to off-white powder. White to off-white suspension with fruity aromatic odour.	 Complies Complies	 Complies Complies	 Complies Complies	
Mean mass	14.0gm ± 5% (Between 13.300g and 14.700g)	14.112g	14.134g	14.070g	
Uniformity of weight(mass) of delivered doses from multidose containers	Not more than two of the individual mass deviate from the average mass by more than 10.0% and none deviates by more than twice the percentage (i.e. 20.0%)	- 7.0% to + 0.5%	- 1.9% to + 1.2%	- 1.7% to + 1.2%	

MICRO LABS LIMITED, VEERASANDRA

PRODUCT | **Placebo for Co- amoxiclav 400/57mg/5ml Sugar Free Powder For Oral suspension**

Batch Number	: PDAHV0001	Strength	: 400/57 mg/5ml
Mfg. Date	: Jul-14	Exp. Date	: Jun-16
Description of primary Pack	: 115 cc/28mm Heavy Weight HDPE bottle (for 70 ml) with 28 mm CRC Cap with pull tab.		
Source of Primary Pack	: Triveni polymers Pvt Ltd, Mold-Rite Plastics Inc.	Pack Size	: 70ml HDPE
Date of Commencement	: 16/07/14		

Test Intervals		0 month	18 months	24 months	36 months
Specification No.		FPS:R:PDAHV:EU01			
Tests	Specification Limits				
pH	Should be between 4.0 and 6.0	4.21	4.16	4.12	
Water content (By KF)	Not more than 10%	2%	3.1%	5%	
Microbiological quality					
A) Total Bacterial Count	Not more than 1000cfu/g	< 10cfu/g	< 10cfu/g	< 10cfu/g	
B) Total Fungal Count	Not more than 100 cfu/g	<10cfu/g	<10cfu/g	<10cfu/g	
C) Pathogenic organisms					
Escherichia coli	Should be absent /g	Absent/g	Absent/g	Absent/g	
Reconstituted time	Not more than 5 minutes	01 minute 10 seconds	03 minutes 21 seconds	02 minutes 52 seconds	

	MICRO LABS LIMITED, VEERASANDRA
PRODUCT	**Placebo for Co- amoxiclav 400/57mg/5ml Sugar Free Powder For Oral suspension**

Batch Number : PDAHV0001 Strength : 400/57 mg/5ml

Mfg. Date : Jul-14 Exp. Date : Jun-16

Description of primary Pack : 115 cc/28mm Heavy Weight HDPE bottle (for 70 ml) with 28 mm CRC Cap with pull tab.

Source of Primary Pack : Triveni polymers Pvt Ltd, Mold-Rite Plastics Inc. Pack Size : 70ml HDPE

Date of Commencement : 16/07/14

Test Intervals		0 month	18 months	24 months	36 months
Specification No.		FPS:R:PDAHV:EU01			
Tests	**Specification Limits**				
Reconstituted suspension after 7days					
Description Reconstituted suspension	White to off-white suspension with fruity aromatic odour.	Complies	Complies	Complies	
pH of the suspension	Should be between 4.0 and 6.0	4.15	4.13	4.15	

Remarks:	Passes	Passes	Passes	
A.R. No.	VFP141755	VMS160029	VMS160386	
Analysis Completed on:	28/01/16	28/01/16	18/07/16	
Specification No. (used for initial analysis):	FPS:R:PDAHV:EU01			

Conclusion: 24 months analysis completed, results found satisfactory.

Approved by:

Head-QA 19/07/16

MICRO LABS	MICRO LABS LIMITED, VEERASANDRA
	QUALITY CONTROL DEPARTMENT
	CERTIFICATE OF ANALYSIS

Product Name	Placebo for Co-amoxiclav 400/ 57 mg/ 5mL Sugar free powder for oral suspension	Page No.	1 of 2
Generic Name	Placebo for Co-amoxiclav 400/ 57 mg/ 5mL Sugar free powder for oral suspension	BMR No.	BMR1:PDAHV:EU01
Specification Reference No.	**FPS:R:PDAHV:EU01**	**Finished Product Code**	**PDAHV;A**
A.R. No.	VMS160386(24months sample)	Batch Size	6,500 Bottles
Batch No.	PDAHV0001	Sampled Qty.	Analysis sample: 15 Bottles
Mfg. Date	07/2014	Expiry Date	06/2016
Sampled By	Ajay	Sampled On	05/07/2016
Date of Report	18/07/2016	Release quantity	NA
Presentation Pack	115 cc/28mm Heavy Weight HDPE bottle (for 70 ml) with 28 mm CRC Cap.		

Test No.	Test	Results	Specifications
Initial analysis			
1	Description i) Dry powder ii) Reconstituted Suspension	 Off-white powder. Off-white suspension with fruity aromatic odour.	 White to off-white powder. White to off-white suspension with fruity aromatic odour.
2	Mean mass	14.070g	14.0 gm ± 5% (Between 13.300 g and 14.700g)
3	Uniformity of weight (mass) of delivered doses from multidose containers	- 1.7% to + 1.2%	Not more than two of the individual mass deviate from the average mass by more than 10.0 % and none deviates by more than twice the percentage (i.e. 20.0%).
4	pH of the suspension	4.12	Should be between 4.0 and 6.0
5	Water content (By KF)	5%	Not more than 10%

L:004:FCA/B

	MICRO LABS LIMITED, VEERASANDRA
MICRO LABS	QUALITY CONTROL DEPARTMENT
	CERTIFICATE OF ANALYSIS

Product Name	Placebo for Co-amoxiclav 400/ 57 mg/ 5mL Sugar free powder for oral suspension	Page No.	2 of 2
Generic Name	Placebo for Co-amoxiclav 400/ 57 mg/ 5mL Sugar free powder for oral suspension	BMR No.	BMR1:PDAHV:EU01
Specification Reference No.	**FPS:R:PDAHV:EU01**	**Finished Product Code**	**PDAHV:A**
Batch No.	PDAHV0001	A.R. No.	VMS160386

Test No.	Test	Results	Specifications
6	Microbiological quality		
	A) Total Bacterial Count	< 10 cfu/g	Not more than 1000 CFU / g
	B) Total Fungal Count	< 10cfu/g	Not more than 100 CFU / g
	C) Pathogenic organisms		
	Escherichia coli	Absent/g	Should be absent /g
7	Reconstituted time	02 minutes 52 seconds	Not more than 5 minutes
Reconstituted suspension after 7 days			
1	Description Reconstituted suspension	Off-white suspension with fruity aromatic odour.	White to off-white suspension with fruity aromatic odour.
2	pH of the suspension	4.15	Should be between 4.0 and 6.0

Remarks: The sample complies / ~~does not comply~~ with specification No.: FPS:R:PDAHV:EU01 with respect to above tests.

	Name	Title	Sign/Date
Prepared by:	B. Seshu Reddy.	Sr. Executive-QC	18/7/16
Checked by:	Akbar Mohandy	Asst. Manager-QA	18/07/16
Approved by: Site QC Head	R. Senthilnathan	G.M. QC	18/07/16
Authorized by: Site QA Head	SATISH BABU V.S	Sr. GM - QA	19/07/16

L:004:FCA/B

MHRA
Regulating Medicines and Medical Devices

MHRA
151 Buckingham Palace Road
London SW1W 9SZ
United Kingdom

www.gov.uk/mhra

Mrs Michelle Biggs
MAWDSLEY-BROOKS & COMPANY LIMITED
UNIT 3
SOUTH LANGWORTHY ROAD
PO BOX 18
SALFORD
M50 2PW
UNITED KINGDOM

MIA(IMP) NUMBER: MIA(IMP) 741 Version: 11

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's Authorisation - Investigational Medicinal Products

SECTION 1A

1. Authorisation Number

MIA(IMP) Number: MIA(IMP) 741

2. Name of Authorisation Holder

MAWDSLEY-BROOKS & COMPANY LIMITED

3. Trading Style

4. Address(es) of manufacturing/importing site(s)
(All authorised sites should be listed if not covered by separate licences)

MHRA SITE NUMBER:	SITE NAME:	ADDRESS:
1686685	MAWDSLEY-BROOKS & COMPANY LIMITED	UNIT 22, QUEST PARK, WHEATLEY HALL ROAD, DONCASTER, DN2 4LT, UNITED KINGDOM

5. Legally registered address of Authorisation Holder

UNIT 3, SOUTH LANGWORTHY ROAD, PO BOX 18, SALFORD, M50 2PW, UNITED KINGDOM

6. Scope of authorisation and dosage forms

See Annex 2

7. Legal basis of authorisation

See Section 1B of authorisation.

8. Name of responsible officer of the competent authority of the member state granting the manufacturing authorisation

Sean Kaiser

MHRA
Regulating Medicines and Medical Devices

SECTION 1A (continued)

9. Date 09/02/2016

10. Annexes attached

Annex 2

Optional Annexes

Annex 4 (Contract Laboratories)

Annex 5 (Name of Qualified Person)

Annex 6 (Name of Responsible Person)

Annex 8 (Manufactured/Imported products)

Annex 9 (Storage Sites)

MHRA
Regulating Medicines and Medical Devices

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's Authorisation - Investigational Medicinal Products

SECTION 1B

1. This authorisation is granted in accordance with the provisions of the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended [S.I. 2004/1031] which implement Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001.

2. It permits the authorisation holder named on page 1 of Section 1 of the authorisation to manufacture, assemble and/or import investigational medicinal products for human use in accordance with Regulation 41 of the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended [S.I. 2004/1031] (as detailed in section 3 of this authorisation) and is subject to the provisions identified on page 2 of Section 1 of this authorisation.

3. In this document a Manufacturers Authorisation for Investigational Medicinal Products may be referred to as MIA(IMP) and the Medicines and Healthcare products Regulatory Agency (acting on behalf of the Licensing Authority as defined in Regulation 6 of The Human Medicines Regulations 2012 (SI 2012/1916) may be referred to as MHRA.

4. The authorisation holder must inform the MHRA, in advance, of any change to the details submitted by him and/or included in this authorisation. All changes must be approved by the MHRA to have effect. If the business should change hands, the company or person taking over the business will have to obtain a new authorisation before commencing the manufacture, assembly or importation of investigational medicinal products.

Attention is drawn to the structure of this authorisation (as detailed on page 4 of Section 1) and to its completeness in accordance with that structure. This is of particular relevance where the holder of the authorisation is using it as evidence to a third party in support of claims to carry out those operations and activities to which this authorisation applies on premises and using personnel covered by this authorisation.

SECTION 1B (continued)

5. Authorisation Structure

This authorisation is divided into three sections.

(a) Section 1 (this section) identifies the authorisation holder and the responsible officer for the issue of the authorisation. This section would not usually be replaced during routine variations of the authorisation unless the authorisation holder details are varied.

(b) Section 2 lists variations to the authorisation. A replacement section 2 will be issued each time the authorisation is varied.

(c) Section 3 contains the details relating to each site named on the authorisation. Where there is more than one site there will be more than one part to Section 3. When a variation is made to the details of a site named in Section 3 the relevant part of Section 3 will be replaced.

(d) The authorisation holder is required to attach to his authorisation any replacement pages issued by MHRA and to mark or destroy superseded pages as to render them invalid.

---

6. Provisions

a) The provisions of Schedule 7 of the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended [S.I. 2004/1031] shall apply to the authorisation. For manufacture and/or assembly Parts 1 and 2 of Schedule 7 apply and for importation Parts 1 and 3 of Schedule 7 apply in accordance with Regulation 40(4) of the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended [S.I. 2004/1031] subject to Regulation 38(2).

MHRA Regulating Medicines and Medical Devices

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's Authorisation - Investigational Medicinal Products

SECTION 2

VARIATION HISTORY

This page will be amended if the licence is varied.

Date	Variation Detail
02/02/2011	Initial Application
03/02/2011	Internal variation to Site 1686685 (Unit 22, Quest Park): amend the site name, add Mrs Emma Thomson as QP & QC and delete Mr Philip Millward
11/02/2011	Internal variation to Site 1686685 (Unit 22, Quest Park): Add sections 1.1.3 (Batch cert of sterile Products), 1.2.2 (Batch cert of non Sterile Products) and 1.4.3 (Other: Batch release of herbals)
14/02/2011	Internal variation to add 2.2.1.1 to site 1686685.
31/07/2012	Variation: Add new QP Miss Jennifer Anne McLaughlin.
21/11/2012	RBI - Variation to change name of site 3163392 to MAWDSLEY-BROOKS & COMPANY LIMITED
11/12/2012	Variation - site 1686685, add Qualified Persons, Ms M C Siruffo and Dr S Yong, remove site contact Mr D Wood, add new site contact Mrs E Thomson. Add storage site 3163392.
21/11/2013	Variation -Site 1686685 remove J A McLaughlin and Mrs Maria Cecilia Siruffo Perez.
11/12/2013	Variation amend site activities, site 1686685.
14/07/2015	Variation to add QP to Site 1686685
09/02/2016	Variation: (Site 1686685) Add Dr Judith A Hoodless as a QP

MIA(IMP) NUMBER: MIA(IMP) 741 MHRA Site No: 1686685 VERSION: 11

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's Authorisation - Investigational Medicinal Products

SECTION 3

ANNEX 2 - SITE INFORMATION

SCOPE OF AUTHORISATION

Name and address of site:

SITE NAME:	MAWDSLEY-BROOKS & COMPANY LIMITED
ADDRESS:	UNIT 22, QUEST PARK, WHEATLEY HALL ROAD, DONCASTER, DN2 4LT, UNITED KINGDOM
MHRA SITE NUMBER:	1686685

Type of products handled

Human Investigational Medicinal Products for phase I, II, III clinical trials (optional)

Authorised operations

Manufacturing Operations of Investigational Medicinal Products (according to Part 1)	Authorised
Importation of Investigational Medicinal Products (according to Part 2)	Authorised

ANNEX 2 – SITE INFORMATION (continued)

Part 1 – MANUFACTURING OPERATIONS OF INVESTIGATIONAL MEDICINAL PRODUCTS

- authorised manufacturing operations include total and partial manufacturing (including various processes of dividing up, packaging or presentation), batch release and certification, importation, storage and distribution of specified dosage forms unless informed to the contrary;
- quality control testing and/or release and batch certification activities without manufacturing operations should be specified under the relevant items;
- if the company is engaged in manufacture of products with special requirements e.g. radiopharmaceuticals or products containing penicillin, sulphonamides, cytotoxics, cephalosporins, substances with hormonal activity or other or potentially hazardous active ingredients this should be stated under the relevant product type and dosage form (applicable to all sections of Part 1 apart from sections 1.5.2 and 1.6)

1.1	**Sterile Investigational Medicinal Products**	**Manufacture**
1.1.1	**Aseptically prepared (processing operations for the following dosage forms)**	
	1.1.1.1 Large volume liquids	Not Authorised
	1.1.1.2 Lyophilisates	Not Authorised
	1.1.1.3 Semi-solids	Not Authorised
	1.1.1.4 Small volume liquids	Not Authorised
	1.1.1.5 Solids and implants	Not Authorised
	1.1.1.6 Other aseptically prepared products	Not Authorised

1.1.2	***Terminally Sterilised (processing operations for the following dosage forms)***	**Manufacture**
	1.1.2.1 Large volume liquids	Not Authorised
	1.1.2.2 Semi-solids	Not Authorised
	1.1.2.3 Small volume liquids	Not Authorised
	1.1.2.4 Solids and implants	Not Authorised
	1.1.2.5 Other terminally sterilised prepared products	Not Authorised
1.1.3	***Batch certification***	Not Authorised

1.2	**Non-sterile investigational medicinal products**	**Manufacture**
1.2.1	***Non-Sterile Products (processing operations for the following dosage forms)***	
	1.2.1.1 Capsules, hard shell	Not Authorised
	1.2.1.2 Capsules, soft shell	Not Authorised
	1.2.1.3 Chewing gums	Not Authorised
	1.2.1.4 Impregnated matrices	Not Authorised
	1.2.1.5 Liquids for external use	Not Authorised
	1.2.1.6 Liquids for internal use	Not Authorised
	1.2.1.7 Medicinal gases	Not Authorised
	1.2.1.8 Other solid dosage forms	Not Authorised
	1.2.1.9 Pressurised preparations	Not Authorised
	1.2.1.10 Radionuclide generators	Not Authorised
	1.2.1.11 Semi-solids	Not Authorised
	1.2.1.12 Suppositories	Not Authorised
	1.2.1.13 Tablets	Not Authorised

	1.2.1.14 Transdermal patches	Not Authorised
	1.2.1.15 Other non-sterile medicinal products	Not Authorised
1.2.2	***Batch certification***	Not Authorised

1.3	**Biological investigational medicinal products**	**Manufacture**
1.3.1	***Biological medicinal products (list of product types)***	
	1.3.1.1 Blood products	Not Authorised
	1.3.1.2 Immunological products	Not Authorised
	1.3.1.3 Cell therapy products	Not Authorised
	1.3.1.4 Gene therapy products	Not Authorised
	1.3.1.5 Biotechnology products	Not Authorised
	1.3.1.6 Human or animal extracted products	Not Authorised
	1.3.1.7 Tissue Engineered Products	Not Authorised
	1.3.1.8 Other biological medicinal products	Not Authorised
1.3.2	***Batch certification***	
	1.3.2.1 Blood products	Not Authorised
	1.3.2.2 Immunological products	Not Authorised
	1.3.2.3 Cell therapy products	Not Authorised
	1.3.2.4 Gene therapy products	Not Authorised
	1.3.2.5 Biotechnology products	Not Authorised

	1.3.2.6 Human or animal extracted products	Not Authorised
	1.3.2.7 Tissue Engineered Products	Not Authorised
	1.3.2.8 Other biological medicinal products	Not Authorised

1.4	***Other investigational medicinal products or manufacturing activity*** (any other relevant manufacturing activity/product type that is not covered above e.g. sterilisation of active substances, manufacture of biological active starting materials (when required by national legislation), medicinal gases, herbal or homeopathic products, bulk or total manufacturing, etc).	**Manufacture**
1.4.1	**Manufacture of:**	
	1.4.1.1 Herbal products	Not Authorised
	1.4.1.2 Homoeopathic products	Not Authorised
	1.4.1.3 Other	Not Authorised
1.4.2	**Sterilisation of active substances/excipients/finished products:**	
	1.4.2.1 Filtration	Not Authorised
	1.4.2.2 Dry heat	Not Authorised
	1.4.2.3 Moist heat	Not Authorised
	1.4.2.4 Chemical	Not Authorised
	1.4.2.5 Gamma irradiation	Not Authorised
	1.4.2.6 Electron beam	Not Authorised
1.4.3	**Others**	Not Authorised

1.5	Packaging	Packaging
1.5.1	Primary packing	
	1.5.1.1 Capsules, hard shell	Not Authorised
	1.5.1.2 Capsules, soft shell	Not Authorised
	1.5.1.3 Chewing gums	Not Authorised
	1.5.1.4 Impregnated matrices	Not Authorised
	1.5.1.5 Liquids for external use	Not Authorised
	1.5.1.6 Liquids for internal use	Not Authorised
	1.5.1.7 Medicinal gases	Not Authorised
	1.5.1.8 Other solid dosage forms	Not Authorised
	1.5.1.9 Pressurised preparations	Not Authorised
	1.5.1.10 Radionuclide generators	Not Authorised
	1.5.1.11 Semi-solids	Not Authorised
	1.5.1.12 Suppositories	Not Authorised
	1.5.1.13 Tablets	Not Authorised
	1.5.1.14 Transdermal patches	Not Authorised
	1.5.1.15 Other non-sterile medicinal products	Not Authorised
1.5.2	Secondary packing	Authorised

1.6	**Quality control testing**	
	1.6.1 Microbiological: sterility	Not Authorised
	1.6.2 Microbiological: non-sterility	Not Authorised
	1.6.3 Chemical/Physical	Not Authorised
	1.6.4 Biological	Not Authorised

Any restrictions or clarifying remarks related to the scope of these Manufacturing operations:

ANNEX 2 – SITE INFORMATION (continued)

Part 2 – IMPORTATION OF INVESTIGATIONAL MEDICINAL PRODUCTS

- authorised importation activities without manufacturing activity
- authorised importation activities include storage and distribution unless informed to the contrary

2.1	**Quality control testing**	**Import**
	2.1.1 Microbiological: sterility	Not Authorised
	2.1.2 Microbiological: non-sterility	Not Authorised
	2.1.3 Chemical/Physical	Not Authorised
	2.1.4 Biological	Not Authorised
2.2	**Batch certification of imported medicinal products**	
2.2.1	***Sterile Products***	
	2.2.1.1 Aseptically prepared	Authorised
	2.2.1.2 Terminally sterilised	Authorised
2.2.2	***Non-sterile products***	Authorised
2.2.3	***Biological medicinal products***	
	2.2.3.1 Blood products	Authorised
	2.2.3.2 Immunological products	Authorised
	2.2.3.3 Cell therapy products	Authorised

	2.2.3.4 Gene therapy products	Authorised
	2.2.3.5 Biotechnology products	Authorised
	2.2.3.6 Human or animal extracted products	Authorised
	2.2.3.7 Tissue Engineered Products	Not Authorised
	2.2.3.8 Other biological medicinal products	Not Authorised
2.3	**Other Importation Activities**	
	2.3.1 Site of Physical Importation	Not Authorised
	2.3.2 Importation of Intermediate which undergoes further processing	Not Authorised
	2.3.3 Other	Not Authorised

Any restrictions or clarifying remarks related to the scope of these importing operations:

ANNEX 5/6 – SITE INFORMATION (continued)

Personnel

Person Number	Name	Personnel Type			
		QP	TQP	PM	QC
128087	Mr Stephen T Garner	Yes	No	No	Yes
1259637	Dr Martin Frederick Jones	Yes	No	No	No
126523	Mr Jeff Cox	Yes	No	No	No
2228891	Miss Kelly Ounsley	No	No	Yes	No
2179527	Mr Philip Millward	Yes	No	No	No
623766	Dr Set Hui Yong	Yes	No	No	No
119278	Mrs E Thomson	Yes	No	No	Yes
135110	Dr Judith A Hoodless	Yes	No	No	No

Key to Roles:

QP – Qualified Person
TQP – Transitional Qualified Person
PM – Production Manager/Supervisor
QC – Person responsible for Quality Control

ANNEX 4 – CONTRACT LABORATORIES

MHRA SITE NUMBER:	LABORATORY NAME:	ADDRESS:
5566	QUALITY CONTROL NORTH WEST	STEPPING HILL HOSPITAL, STOCKPORT, SK2 7JE, UNITED KINGDOM
12378	MINERVA SCIENTIFIC LIMITED	DELVES ROAD, HEANOR GATE, DE75 7SG, UNITED KINGDOM
28874	EXOVA (UK) LIMITED	LOCHEND INDUSTRIAL ESTATE, NEWBRIDGE, EH28 8PL, UNITED KINGDOM

ANNEX 9 – STORAGE SITES

MHRA SITE NUMBER:	SITE NAME:	ADDRESS:
1686685	MAWDSLEY-BROOKS & COMPANY LIMITED	UNIT 22, QUEST PARK, WHEATLEY HALL ROAD, DONCASTER, DN2 4LT, UNITED KINGDOM
3163392	MAWDSLEY-BROOKS & COMPANY LIMITED	QUEST 90, QUEST PARK, WHEATLEY HALL ROAD, DONCASTER, DN2 4LT, UNITED KINGDOM
89833	MAWDSLEY BROOKS & COMPANY LIMITED	FINGLE DRIVE, STONEBRIDGE, MILTON KEYNES, MK13 0DN, UNITED KINGDOM
91444	MAWDSLEY BROOKS & COMPANY LIMITED	PARKWAY DRIVE, UNIT 7, PARKWAY ONE BUSINESS CENTRE, SHEFFIELD, S9 4WU, UNITED KINGDOM
93570	MAWDSLEY BROOKS & COMPANY LIMITED	UNIT 3, SOUTH LANGWORTHY ROAD, SALFORD, M50 2PW, UNITED KINGDOM

MHRA
Regulating Medicines and Medical Devices

MHRA
151 Buckingham Palace Road
London SW1W 9SZ
United Kingdom

mhra.gov.uk

Ms T Carver
UNIVERSITY OF OXFORD
DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES
23-38 HYTHE BRIDGE STREET
OXFORD
OX1 2ET
UNITED KINGDOM

22/09/2016

Dear Ms T Carver

THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 2004/1031

Our Reference:	21584/0321/001-0003
Eudract Number:	2013-002822-21
Product:	BROWN & BURK Co-amoxiclav Oral Suspension 400 mg/57 mg/5 ml
Protocol number:	ARCHIE001
Substantial Amendment Code Number:	Code Number: ARCHIE_SA014
Version:	
Date: 2016/09/13	

ACKNOWLEDGEMENT OF AMENDMENT

Thank you for your notice of amendment, received on 20/09/2016. The information you provided to support your request is complete and therefore your request is valid.

Your request will be assessed and you will be notified of the Licensing Authority's decision within 35 days.

Please quote the EudraCT number, CTA number and your amendment code in any further communications relating to this submission.

Yours sincerely,

Submissions
MHRA

MHRA
Regulating Medicines and Medical Devices

MHRA
151 Buckingham Palace Road
London SW1W 9SZ
United Kingdom

mhra.gov.uk

Ms T Carver
UNIVERSITY OF OXFORD
DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES
23-38 HYTHE BRIDGE STREET
OXFORD
OX1 2ET
UNITED KINGDOM

03/10/2016

Dear Ms T Carver

THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 2004/1031

Our Reference:	21584/0321/001-0003
Eudract Number:	2013-002822-21
Product:	BROWN & BURK Co-amoxiclav Oral Suspension 400 mg/57
mg/5 ml	
Protocol number:	ARCHIE001
Substantial Amendment Code Number:	Code Number: ARCHIE_SA014
Version:	
Date: 2016/09/13	

NOTICE OF ACCEPTANCE OF AMENDMENT

I am writing to inform you that the Licensing Authority accepts the proposed amendment to your clinical trial authorisation (CTA), received on 20/09/2016.

This amendment may therefore be made.

You are reminded that where it is appropriate, the Ethics Committee should also be notified of amendments.

Yours sincerely,

Clinical Trials Unit
MHRA

Primary Health Care Archie

From: AMENDMENTS, hra (HEALTH RESEARCH AUTHORITY) <hra.amendments@nhs.net>
Sent: 11 November 2016 13:39
To: Primary Health Care Archie
Cc: Kay Wang; Karl Shepherd
Subject: RE: IRAS 121769. Confirmation of Assessment outcome

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Sharon,

Further to the below, I am pleased to confirm that HRA Approval has been issued for the referenced amendment, following assessment against the HRA criteria and standards.

The sponsor should now work collaboratively with participating NHS organisations in England to implement the amendment as per the below categorisation information. This email may be provided by the sponsor to participating organisations in England to evidence that the amendment has HRA Approval.

Please contact hra.amendments@nhs.net for any queries relating to the assessment of this amendment.

Yours sincerely,
Simon

Simon Connolly | Senior Assessor
Health Research Authority
Ground Floor | Skipton House | 80 London Road | London | SE1 6LH
E: simon.connolly1@nhs.net | T: 020 7972 2552

Would you like to receive the latest updates on HRA work? Sign up here

For more information on the HRA Approval process Click here

From: amendments hra (HEALTH RESEARCH AUTHORITY)
Sent: 08 November 2016 15:56
To: 'Primary Health Care Archie'
Cc: 'kay.wang@phc.ox.ac.uk'; 'karl.shepherd@admin.ox.ac.uk'
Subject: IRAS 121769. Confirmation of Amendment Categorisation as Category C

Dear Sharon,

IRAS Project ID:	121769
Short Study Title:	The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE
Date complete amendment submission received:	**31/10/2016**
Amendment No./ Sponsor Ref:	ARCHIE_SA014
Amendment Date:	13/09/2016
Amendment Type:	**Substantial for information only**

Thank you for submitting the above referenced amendment. In line with the UK Process for Handling UK Study Amendments I can confirm that this amendment has been categorised as:

Category C - An amendment that has no implications that require management or oversight by the participating NHS organisations

As such, the sponsor may implement this amendment **as soon as any relevant regulatory approvals are in place** (for participating organisations in England, please see 'Confirmation of Assessment Arrangements' below).

As Chief Investigator/Sponsor, it remains your responsibility to ensure that the research management offices and local research teams (if applicable) at each of your participating organisations are informed of this amendment.

Note: you may only implement changes described in the amendment notice or letter.

Participating NHS Organisations in England – Confirmation of Assessment Arrangements

Further to the details above, I can confirm that this amendment will be assessed by the HRA to confirm that it meets the expected criteria and standards. An Assessor from the HRA will contact you, and you will receive separate notification that the HRA Assessment is complete. You should not implement this amendment at participating NHS organisations in England until the outcome of the HRA assessment is confirmed, and the conditions detailed in the categorisation section above have been met.

Please do not hesitate to contact me if you require further information.

Kind regards

Laura Greenfield

Laura Greenfield | Amendments Coordinator
Health Research Authority

Research Ethics Service (RES)
HRA, The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS
E: hra.amendments@nhs.net

T: 020 7104 8096
www.hra.nhs.uk

NHSmail provides an email address for your career in the NHS and can be accessed anywhere
For more information and to find out how you can switch, visit www.nhsdigital.nhs.uk/nhsmail

****
****

North West - Liverpool East Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Tel: 0207 104 8004

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

16 November 2016

Dr Kay Wang
University of Oxford
Radcliffe Observatory Quarter
Woodstock Road
Oxford
OX2 6GG

Dear Dr Wang,

Study title:	**The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care(ARCHIE): a double-blind randomised placebo-controlled trial**
REC reference:	**13/NW/0621**
Protocol number:	**ARCHIE001**
EudraCT number:	**2013-002822-21**
Amendment number:	**14**
Amendment date:	**13 September 2016**
IRAS project ID:	**121769**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper		20 September 2016
Investigator's brochure / IMP Dossier [Clean]	3	07 September 2016
Investigator's brochure / IMP Dossier [Tracked]	3	07 September 2016
Notice of Substantial Amendment (CTIMP)	14	13 September 2016
Other [MHRA Acknowledgment]		22 September 2016
Other [MHRA Confirmation of Acceptance]		03 October 2016
Other [sponsor authorization]		16 September 2016

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R&D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

13/NW/0621: Please quote this number on all correspondence

Yours sincerely

Signed on behalf of:
Mrs Glenys J Hunt
Chair

E-mail: nrescommittee.northwest-liverpooleast@nhs.net

Copy to: Ms Heather House, Oxford University NHS Trust

North West - Liverpool East Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 09 November 2016