Appendix 1: Authentication Certificate of *Eugenia jambolana* (seeds), *Momordica charantia* (fruit) and *Gmelina arborea* (bark)

Appendix 2: GMP and ISO Certificate of extract manufacturing facility

Appendix 3: Ethics Committee Approvals
Authentication Certificate

We have studied macroscopically, microscopically and organoleptically the sample submitted by Mr. Pramod Kashid, SPTM NMIMS university, Mumbai - 400 672.

We hereby authenticate that the sample belongs to bark of *Gmelina arborea* Roxb. (Family- Verbenaceae).

The certificate is issued at his request and given only for academic use.

(A.M. Mujumdar)
Head, Plant Sciences Division

Head, Plant Sciences Division,
Agharkar Research Institute,
Pune 411 004
Authentication Certificate

We have studied macroscopically and organoleptically the sample submitted by Mr. Pramod Kashid, SPTM NMIMS university, Mumbai - 400 672.

We hereby authenticate that the sample belongs to seeds of Syzygium cumini (L.) Skeels (= Eugenia jambolana Lam.) Family- Myrtaceae.

The certificate is issued at his request and given only for academic use.

(A.M. Mujumdar)
Head, Plant Sciences Division

Head, Plant Sciences Division,
Agharkar Research Institute,
Pune 411 004

Auth.09-114
Authentication Certificate

We have studied macroscopically and organoleptically the sample submitted by Mr. Pramod Kashid, SPTM NMIMS university, Mumbai - 400 672.

We hereby authenticate that the sample belongs to fruits of *Momordica charantia* Linn. (Family - Cucurbitaceae).

The certificate is issued at his request and given only for academic use.

(A.M. Mujumdar)
Head, Plant Sciences Division

Head, Plant Sciences Division,
Agharkar Research Institute,
Pune 411 004

Auth.09-113
Appendix II
No. Certi/PHYTO/2010/13605/D/Ayu
Commissioner,
Food & Drugs Control Administration,
Block No. 8, 1st Floor,
Dr. Jivraj Mehta Bhavan,
GANDHINAGAR.
Date: 19 Jun 2010

G.M.P. CERTIFICATE
FORM 26-E-1
(SEE RULE 155-B)
(CERTIFICATE OF GOOD MANUFACTURING PRACTICES (G.M.P.) TO MANUFACTURE AYURVEDA, SIDDHA & UNANI DRUGS)


THIS CERTIFICATE IS VALID FOR A PERIOD OF FIVE YEARS FROM THE DATE OF ISSUE.

Joint Commissioner (Ayurved),
Food & Drugs Control Administration
Gujarat State, Gandhinagar.
11/06/2010
Certificate of Conformity

This is to certify that the Manufacturing practices of the following organization has been assessed by Intertek and found to comply with the requirements of:

HACCP-INTERNATIONAL CODE OF PRACTICE GENERAL PRINCIPLES OF FOOD HYGIENE CAC/RCP 1-1969, Rev. 4-2003

Confirmation Number: CONFHACCP10003

Organization:

Phyto Concentrates

Plot No. 1145, Industrial Estate, Santej, Ta. Kalol, Dist-Gandhinagar, Gujarat (India) Pin-382721

HACCP is applicable to:

Manufacturing, storage and dispatch of Herbal Extracts and Ayurvedic Formulations

Confirmation issue date: July 02, 2010
Confirmation expiry date: July 01, 2011
Date of Evaluation: February 26, 2010
Re-evaluation due date: February 25, 2011

Authorized Signatory

2nd July 2010
Certificate of Registration

The following organization’s Food Safety management system has been assessed and registered by Intertek Semko Certification AB as conforming to the requirements of:

ISO 22000:2005

Organization:

Phyto Concentrates

Plot No. 1145, Industrial Estate, Santej, Ta. Kalol, Dist- Gandhinagar, Gujarat (India) Pin-382721

The Food Safety Management System is applicable to:

Manufacturing, storage and dispatch of Herbal Extracts and Ayurvedic Formulations

In the issuance of this certificate, Intertek assumes no liability to any party other than to the Client, and then only in accordance with the agreed upon Certification Agreement.

Intertek Semko Certification AB - Kista (Stockholm), Sweden
Part B

PROTOCOL FORM FOR RESEARCH PROPOSALS TO BE SUBMITTED TO THE COMMITTEE/ INSTITUTIONAL ANIMAL ETHICS COMMITTEE, FOR NEW EXPERIMENTS OR EXTENSIONS OF ONGOING EXPERIMENTS USING ANIMALS OTHER THAN NON-HUMAN.

1. Project title: "Pharmacological Studies on Selected Herbs as Antidiabetic Agents"

2. Chief Investigator(s):
   1. Name : Ms. Pramod Kashid (Industry - Trident Clinical Research)
   2. Name : Dr. (Mrs.) Rumi Ghosh.
      Designation : Assistant Professor
      Dept/Div/Lab : Department of pharmacology
                     Bharati Vidyapeeth's college of pharmacy
                     Navi Mumbai

3. List of name of all individuals authorized to conduct procedures under this proposal.
   ➢ Pramod Kashid (Industry - Trident Clinical Research)
   ➢ Mr. Sagar M. Patil (M Pharm student)

4. Funding Source: Self

5. Duration of the project:
   a. Number of months- 8.
   b. Date of initiation- September 2009.
   c. Date of completion- May 2010.
6. If date by which approval is needed is less than six weeks from date of submission,
   - Justification for the same - Not Applicable.

7. Study Objectives-

   The objectives of present project is to investigate safety and anti-diabetic effects of the selected herbal drugs. The studies involved are:
   2. Study of insulin potentiating effect of selected herbs.
   3. Acute toxicity test in normal mice.
   4. Repeated Dose toxicity study.

8. Animals required:
   - Number of animal required for the project

<table>
<thead>
<tr>
<th>Name of the Experiment</th>
<th>Animal Species</th>
<th>Number of Animal required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alloxan induced diabetes</td>
<td>Wistar Rat</td>
<td>48</td>
</tr>
<tr>
<td>Acute Toxicity</td>
<td>Swiss Albino Mice</td>
<td>30</td>
</tr>
<tr>
<td>Repeated Dose toxicity study</td>
<td>Wistar Rat</td>
<td>50</td>
</tr>
<tr>
<td>Insulin Potentiating Effect</td>
<td>Wistar Rat</td>
<td>20</td>
</tr>
</tbody>
</table>

9. Rationale for animal usage:
   a. Why is animal usage necessary for the study?
In preclinical screening of drug, as reported in the standard methods of screening the studies with animals are necessary.

b. Why are the particular species selected required?
- In the present study, we have selected rat & mice, as standard model for evaluating safety and antidiabetic activity. Result obtained in these model correlates with clinical observation in human beings.

c. Why are the estimated numbers of animals essential?
- Standard procedure specifies 5-6 animals to be included in each group to avoid biological variation and to obtain sufficient data for statistical evaluation. Journals do not accept research work if study is conducted using less than 6 animals per group.

d. Have similar experiments conducted in the past. If so, the number of animals used and results obtained in brief?
- No.

e. If yes, why new experiment is required?
- Not applicable.

f. Have similar experiment(s) been made by any other organization / agency? If so, their results in your knowledge.
- Similar experiments have not been carried out by any other organization to the best of my knowledge.

10. Description of procedures to be used:
- Not Details attached

11. Dose the protocol prohibit use of anesthetics or analgesic for the conduction of painful Procedures
- Not applicable.

12. Will survival surgery be done?
- No.

13. Method of disposal post experimentation:
- Dead animals will be disposed off by putting them in pit in the ground.
  To be dug for this purpose
14. Animal transportation methods if extra institutional transport is envisaged:
   ➢ Animal shall be transported as per CPCSEA norms for transportation of animals in Auto rickshaw

15. Use of hazardous agents:
   ➢ Not used.

INVESTIGATOR

Pramod Kashid

SIGNATURE
INVESTIGATOR'S DECLARATION:-

1. I certify that I have determined that the research proposal herein is not unnecessarily duplicative of previously reported research.

2. I certify that all individuals working on this proposal, and experimenting on the animals, have been trained in animal handling procedures.

3. For procedures listed under item 11, I certify that I have reviewed the pertinent Scientific Literature and have found no valid alternative to any procedure described herein which might cause less pain or distress.

4. I will obtain approval from the IAEC/CPCSEA before initiating any significant changes in this study.

5. Certified that performance of experiment will be initiated only upon review and approval of scientific intent by appropriate expert body (institutional scientific advisory Committee/ funding agency/other body.)

6. Institutional Biosafety Committee's certification of review and concurrence will be taken.

7. I shall maintain all the records as per format (form D).

Date 02.06.2009

Signature.

(Pramod Kashid)

(For IAEC / CPCSEA usage) 762/03/CPCSEA/25

Proposal number-

Date first received-

Date received after modification (if any)

Date received after second modification (if any)

Approval date

Expiry date

Name of IAEC/CPCSEA Chairperson

Date 03. Aug. 2009

Signature

Chairperson (IAEC)
30-Dec-2009

To,

Dr. Pramod Kashid,

Trident Clinical Research
Mumbai

Title of the Study:

A multicentric prospective randomized, single blind, dose optimization study to evaluate the efficacy and safety of Eugenia jambolana and *Momordica charantia* following multiple dose administration in subjects diagnosed with NIDDM

**Protocol Id:** CT/EJMC/001, Version 01, Nov-2009.

**Subject:** Your letter dated 18-Dec-2009 for review of study documents

Dear Mr. Kashid,

The meeting of the Human Research Independent Ethics Committee (HRIEC) was held on 28-Dec-2009 at 06.30 pm to 08.30 pm at 6/6/4/4, Sector 3, CBD Belapur, Navi Mumbai. The IEC reviewed the below mentioned clinical study and approved the following documents submitted for this study at the meeting.

2. Participant Information and Consent form in English, Version 1.0, 03-Dec-2009
3. Participant Information and Consent form in Hindi translated on 14-Dec-2009 from Participant Information and Consent form in English, Version 1.0, Dated 03-Dec-2009
5. Draft copy of Case Record Form, Version 1.0, 10-Dec-2009
6. CVs of investigators Dr. Tamboli, Dr. Kashid and Yadav

The Committee approved the study to be conducted at following three sites:
1. Dr. Saifun Tamboli, Tamboli Hospital and Research Centre, Sangola, Dist: Solapur
2. Dr. Vijay Kashid, Yashodha Multispecialty Hospital, Main Road Songola, Dist Solapur
3. Dr. Chandrakant Yadav, Smriti Clinic, Mankhurd, Mumbai

The list of members who attended the meeting held on 28-Dec-2009 is as follows:

Name of the Chairperson at the meeting: Mr. Rahul Mali

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Name</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mr. Rahul Mali</td>
<td>Chairperson</td>
</tr>
<tr>
<td>2</td>
<td>Dr. Amol Hule</td>
<td>Member Secretary, Pharmacologist</td>
</tr>
<tr>
<td>3</td>
<td>Mr. Bharat Naravar</td>
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<tr>
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<td>Medical Scientist, Deputy Chairperson</td>
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<td>Legal Expert</td>
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<tr>
<td>12</td>
<td>Mr. Sachin Boraste,</td>
<td>Layperson</td>
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<td>Ms. Rima Mote</td>
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<tr>
<td>14</td>
<td>Ms. Rupali Naravar</td>
<td>Social Worker</td>
</tr>
</tbody>
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It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.
The IEC hereby approves the proposal entitled, Protocol CT/EJMC/001, Version 01, Nov-2009, “A multicentric prospective randomized, single blind, dose optimization study to evaluate the efficacy and safety of Eugenia jambolana and Momordica charantia following multiple dose administration in subjects diagnosed with NIDDM.”

No deviations from or changes of the protocol and Informed Consent Form should be initiated without prior written approval / favorable opinion of the IEC except when necessary to eliminate immediate hazards to the subject, or when changes involve only logistic or administrative types. The approval is valid till for the entire duration of the study.

During the conduct of the study, IEC must be informed about the followings:

- Safety information: Any SAE occurring during the course of the study at the study facility, reports of unexpected serious adverse drug reactions, any new information which may adversely affect the safety of the subjects or the conduct of the trial.

- Any amendment to the protocol, Informed consent form.

- Progress of the study annually or at the end of the study whichever is earlier.

- A copy of the final report should be submitted to the IEC for review.

We confirm that IEC is constituted and functions as per the Good Clinical Practice issued by the Central Drugs Standard Control Organization (CDSCO), Schedule Y of Drug and Cosmetic Acts 1940 and its amendments 20th January 2005 and Ethical Guidelines for Biomedical Research on human subjects published by ICMR. ICH GCP guidelines and declaration of Helsinki 1964 and its amendments.

Mr. Rahul Mali,
Chairman, IHREC
01-May-2010

To,

Dr. Pramod Kashid,

Trident Clinical Research
Mumbai

Title of the Study:

A multicentric prospective randomized, single blind study to evaluate the efficacy and safety of *Eugenia jambolana* and *Momordica charantia* following multiple dose administration in subjects newly diagnosed with NIDDM


Subject: Your letter dated 15-Apr-2010 for review of study documents

Dear Mr. Kashid,

The meeting of the Human Research Independent Ethics Committee (HRIEC) was held on 30-Apr-2010 at 07.00 pm to 09.00 pm at F6/6/4/4, Sector 3, CBD Belapur, Navi Mumbai. The IEC reviewed the below mentioned clinical study and approved the following documents submitted for this study at the meeting.

2. Participant Information and Consent form in English, Version 1.0,
3. Participant Information and Consent form in Hindi translated on 05-Apr-2010 from Participant Information and Consent form in English, Version 1.0, Dated 01-Apr-2010
5. Draft copy of Case Record Form, Version 1.0, 10-Apr-2010
6. Published details/References of test preparations.
7. CVs of investigators Dr. Tamboli, Dr. Kashid

The Committee approved the study to be conducted at following three sites:
1. Dr. Saifun Tamboli, Tamboli Hospital and Research Centre, Sangola, Dist: Solapur
2. Dr. Vijay Kashid, Yashodha Multispecialty Hospital, Main Road Songola, Dist Solapur

The list of members who attended the meeting held on 30-Apr-2010 is as follows:

Name of the Chairperson at the meeting: Mr. Rahul Mali

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<td>14</td>
<td>Ms. Rupali Narnavar</td>
<td>Social Worker</td>
</tr>
</tbody>
</table>

It is hereby confirmed that neither you nor any of the study team members have
participated in the voting/decision making procedures of the committee.

The IEC hereby approves the proposal entitled, Protocol CT/EJMC/002, Version 01, 245-Mar-2010, "A multicentric prospective randomized, single blind study to evaluate the efficacy and safety of Eugenia jambolana and Monordica charantia following multiple dose administration in subjects newly diagnosed with NIDDM"

No deviations from or changes of the protocol and Informed Consent Form should be initiated without prior written approval / favorable opinion of the IEC except when necessary to eliminate immediate hazards to the subject, or when changes involve only logistic or administrative types. The approval is valid till for the entire duration of the study.

During the conduct of the study, IEC must be informed about the followings;

➢ Safety information: Any SAE occurring during the course of the study at the study facility, reports of unexpected serious adverse drug reactions, any new information which may adversely affect the safety of the subjects or the conduct of the trial.

➢ Any amendment to the protocol, Informec consent form.

➢ Progress of the study annually or at the end of the study whichever is earlier.

➢ A copy of the final report should be submitted to the IEC for review.

We confirm that IEC is constituted and functions as per the Good Clinical Practice issued by the Central Drugs Standard Control Organization (CDSCO), Schedule Y of Drug and Cosmetic Acts 1940 and its amendments 20th January 2005 and Ethical Guidelines for Biomedical Research on human subjects published by ICMR. ICH GCP guidelines and declaration of Helsinki 1964 and its amendments.

Mr. Rahul Mali,
Chairman, IHREC