Subject Information Sheet (SIS)

Protocol Title: **Clinical Evaluation of Ashwagandha Standardized Extract (KSM66) for its Pharmacological Actions on Sleep in Subjects Having Insomnia and Healthy Subjects: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study**

Study Code: DYP-Pharm-WS-02-2018; Version-1.1, dt. 20 April 2018

Name of the Subject : _____

Doctor's Name : Dr. Deepak Langade

Institute Name : D. Y. Patil University Medical College & Hospital
Sector – 7, Nerul, Navi Mumbai

1. Introduction:

Insomnia is a major health concern and it may be associated with situational disturbances, poor sleep habits, psychological conditioning, psychiatric disorders (e.g., mood and anxiety disorders), medical disorders, other underlying sleep disorders (e.g. sleep-disordered breathing, restless legs syndrome and circadian rhythm disorders), and stimulating medication effects. Some people may have a primary insomnia not due to external factors. Several risk factors for insomnia have been identified including older age, female gender, divorced or separated adults, lower education, unemployment, and medical illness. Epidemiological surveys confirm that insomnia is a very common problem. Insomnia and anxiety disorders are highly prevalent and are associated with significant impairment and disability. There is evidence that insomnia and anxiety disorders commonly co-occur.
General surveys typically show that about a third to a half of the adult population has at least occasional difficulty with insomnia and 10-20% of adults have insomnia symptoms chronically. The prevalence of insomnia tends to increase with age. One survey conducted in four European countries found that 19% of 15000 people who were interviewed experienced insomnia with some degree of daytime impairment, and that most of them had their symptoms for >6 months.
Animal and human studies have demonstrated that Ashwagandha has anti-anxiety and mood-elevating capabilities.
In assessing response to therapy, actigraphy has proven useful as an outcome measure in patients with insomnia. Actigraphy uses a portable device to record movement over extended periods, making it highly useful to study sleep. In older adults (including older nursing home residents), in whom traditional sleep monitoring can be difficult, actigraphy is indicated for characterizing sleep and to document treatment responses. Similarly, in normal infants and children, as well as special pediatric populations, actigraphy has proven useful for delineating sleep patterns and documenting treatment responses.

This study was planned to assess efficacy of KSM66 Ashwagandha (*Withania somnifera*) on sleep in patients with insomnia and healthy subjects without insomnia.

2. Purpose of the trial:

The clinical research study in which your participation is proposed aims to evaluate Efficacy and Safety of KSM66 Ashwagandha (*Withania somnifera)* in patients with Insomnia, Anxiety: Prospective, Double–Blind, Randomized, Placebo-controlled, Multi-Center Study.

This is a prospective, randomized, double-blind, placebo-controlled study.

Prospective means that you would be given therapy and we would observe the effects of therapy after starting the study therapy.

Randomized means that you would be given therapy in a random manner, i.e. you may receive either 'Ashwagandha therapy' or a 'Placebo therapy' during the entire study period.

Double-blind means that both you and your attending doctor will not be aware of the treatment received by you, i.e. whether it is 'Ashwagandha therapy' or 'Placebo therapy'. This type of blinding helps us reduce the bias and error in the results of the study.

Placebo means that the capsules will not contain Ashwagandha but some other inactive substance. By use of the placebo, we come to know whether the positive results are because of Ashwagandha or are because of psychological factors.

Placebo-controlled means that we compare the results of 'Ashwagandha therapy' with 'Placebo therapy'. Thus, placebo here acts like a control or a reference with which Ashwagandha is compared.

It is expected that you will be benefited with this medicine. On agreeing to participate in this study, you hereby willfully agree to undertake the study activities and medication schedule as required by the study.

The knowledge gained from this study would be of benefit to many thousands of patients, who, like you may suffer from this kind of medical condition.

3. Procedure to be followed:

In this study a total of 80 patients will be enrolled of which 40 shall be healthy subjects (Arm-A) and 40 subjects with insomnia (Arm-B). There would be two blocks of 40 each one for Arm-A and one for Arm-B. At the initial visit, prospective patients would be screened for enrollment based on the requirements of the study, history and clinical examination.

Before starting any study related procedures, you would be explained about the study in details and a written informed consent would be obtained from you to participate in this study. This document is a part of the written informed consent procedure.

A detailed medical history including the associated conditions will be recorded. A general and physical examination would be done to see any abnormal parameters.

If you satisfy the eligibility criteria you would be enrolled in the study.

After enrollment in the study, you will have to take one capsule of KSM 66 Ashwagandha (300 mg) or one capsule of placebo daily with water for a period of 6 weeks (42 days). There is a 50% chance that instead of 'Ashwagandha capsule' you would receive 'Placebo capsule'. This placebo capsule will be identical in size, shape and color with the 'Ashwagandha capsule'

You will be monitored throughout study. After the initial visit, you will have to visit the clinic for assessment at week 1, week 3, and week 6. During each visit, assessments and complete general examination would be done. Side effects will be monitored during each visit of the study period. The study will complete after 6 weeks.

4. Potential Risks of participating in the study

As with all new and old medicines there may be some unforeseen risks associated with this treatment. Care has been taken to design the study to minimize any possible harm, with appropriate screening tests and examinations by the doctor.

The doctor in-charge / attending doctor of the study would explain all other risks associated with the study medication to you.

The efficacy and safety of the drug in this study has been well established and these drugs are being used for long time. Hence, it is unlikely that you may experience any side effects with the study treatment in the dose that you would take in the study.

5. Benefits of the study:

The study therapy may benefit you for insomnia & anxiety. It is therefore possible that it may improve your symptoms due to insomnia. The study medication would be provided free of cost to you by the Sponsor. However, no compensation would be given to you for travelling to the study clinic / hospital and loss of wages / income because of your visit to the clinic.

The knowledge gained from this study would be of benefit to many thousands of patients, who, like yourself, may suffer from this kind of medical condition.

For participation in the study, insurance cover would be provided to you to take care of any medical expenses and compensation in case of any unfortunate incidence due to your participation in the study.

6. Alternative treatments:

There is no evidence for long-term efficacy of currently approved pharmacological treatments in insomnia. The results indicate that the nutritional supplement may improve cognitive performance in elderly with memory complaints.

Currently available symptomatic treatments for insomnia are various drugs with complex activity. But these are not found to be of great use in insomnia.

7. Confidentiality of the record:

Your medical records that are related to this trial will be maintained in confidentiality. The medical monitor and quality assurance representatives from Sponsor (Shri Kartikeya Pharma) may examine your medical records as long as your name cannot be identified from these records.

Your records from this trial may be submitted by the Sponsor to the Government Authorities who control the drugs in the state and the country, but your name will not be identified from such records. No identity of any specific patient in this trial will be disclosed in any public reports or publications.

The authority has the right upon proper judicial order to review pertinent medical records and other data with your name identified. They are required by law; however, the information will be handled in confidential manner.

8. Your Participation in the Study and your Rights

Your participation in this study is voluntary and you may withdraw from the study any time without having to give reasons for the same. In any case, you will be given proper treatment for your condition. Your refusal to participate will not involve any penalty in terms of subsequent participation in research studies. You will agree to cooperate fully with the attending doctor. If at any time you feel worse or suffer any other illnesses, then please inform your attending doctor. If the treatment appears to be unsuitable for you it will be stopped. It is possible that the study could be stopped without your consent. Your doctor will tell you if any new information becomes known during the study, which may affect your willingness to continue in the study.

If you suffer from any treatment related injury during the study, the Sponsor will pay the medical expenses for the treatment of that injury. No other compensation is available from Sponsor.

9. **If you have any queries related to the drug information and safety, you can contact the investigator of the study**

Dr. Deepak Langade
Prof. & Head, Dept. of Pharmacology
D. Y. Patil University Medical College & Hospital
Sector – 7, Nerul, Navi Mumbai – 400 706
Ph: (91) 22 2770 9218 Extn. 166
Cell: 99305 50009
Mail: deepak.langade@dypatil.edu

10. **If any problem develops, you can contact the investigator**

If any serious problems develop, you will receive prompt and appropriate medical attention. It is agreed that the facilities of above-mentioned hospital will be made available to you.

Reasonable medical treatment will be free when provided through above-mentioned hospital.

Financial compensation is not available for medical treatment elsewhere, loss of work, or other expenses.

11. **If you have any queries related to ethical issues & your rights, you can contact the following**

Dr. Krishnat Yadav
Member Secretary
Institutional Ethics Committee (IEC)
D. Y. Patil University Medical College & Hospital
Sector – 7, Nerul, Navi Mumbai – 400 706
Ph: (91) 22 2770 9218 Extn. 132
Cell: 93247 89918
Mail: krishnat.yadav@dypatil.edu

12. **Financial consideration:**

No cost will be incurred by the patients for participating in this study. Patient will not get any financial incentive for participating in this trial.

13. **Obtaining additional information:**

You are encouraged to ask any questions that occur to you at this time or to ask question at any time during your participation in the trial. You will be given a copy of this document for your own information. If you desire more information at a later date you may call the investigator or any member of the study team at the site.

14. **Signature**

I have read the above information and have had opportunity to ask any questions and all of my questions have been answered.

I am also aware of my right to opt out of the trial at any time during trial without having to give reason for doing so.

I have been given a copy of the information sheet & consent form.

Name of Patient _____

Signature/ Thumb impression _____ **Date:** _____

Impartial witness Name_____

Signature _____ **Date: _____**

I the undersigned have fully explained in local language the relevant details of this trial to the patient named above and/or authorized to consent for the patient. I am qualified to perform this role.
(In Case of Illiterate Pts)

Name of Investigator:

Signature _____ **Date: _____**

Informed Consent Form (ICF)

Clinical Evaluation of Ashwagandha Standardized Extract (KSM66) for its Pharmacological Actions on Sleep in Subjects Having Insomnia and Healthy Subjects: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study

Study Code: DYP-Pharm-WS-02-2018, Version-1.0, dt. 09 April 2018

Patient Name: _____

Age: |_|_|_| years or DOB |_|_| / |_|_| / |_|_|

Patient Initials: |_|_|_|

Sr.		Patient Initials
1.	I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions.	
2.	I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without having any medical or legal rights being affected.	
3.	I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any future research that may be conducted in relation to it, even if he/she withdraws from the trial. I agree to this access. However, I understand that his/her identity will not be revealed in any information released to third parties or published.	
4.	I agree not to restrict the use of any data or results that arise from this study.	
5.	I hereby agree to take part in the above study	
6.	I have been informed about the procedures and number of visits of the above referenced study in detail in Patient Information Sheet (This study is a 4-5 visit study spread over 6 weeks treatment)	
7.	I have been explained about the potential risks and benefits (in Patient Information Sheet).	

Signature/Thumb impression of Patient: _____ Date: _____

Sign of the investigator:_____ Date:_____

Signature of Impartial Witness: _____ Date: _____
(In Case Of Illiterate Pts)