

**CAPRISA 054: A pilot study to assess feasibility of
utilizing a prototype Wisebag for enhancing
measurement of gel use in CAPRISA 004**

Principal Investigator

**Dr Leila E. Mansoor, B.Pharm, PhD
CAPRISA, University of KwaZulu-Natal**

Manufacturer of Wisebag :

Wisepill®, CapeTown, South Africa

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Table of Contents

List of Investigators	3
1. Background	4
2. Pilot Study Purpose	4
3. Prototype Wisebag Description	5
Figure 1: Wisebag Dispenser	5
4. Study Timeline, Sample Size and Sites	6
4.1 Pilot Study Timeline	6
4.2 Sample size	6
4.3 Study sites	6
5.0 Participant Selection Process	7
6.0 Standardized messaging to participants:	7
7.0 Proposed future application for the Wisebag	8
References:	9
Appendix 1	10
Wisebag Feasibility Study Informed Consent Form.....	10
Appendix 2: Acceptability Assessment	12

List of Investigators

<p>Principal Investigator: Dr Leila E Mansoor, B.Pharm, PhD 2nd Floor, Doris Duke Medical Research Institute Nelson R Mandela School of Medicine University of KwaZulu-Natal 719 Umbilo Road Congella 4013 South Africa Tel Number: +27 31 260 4641 Fax number: + 27 31 2604566 Email: mansoor@ukzn.ac.za</p>	<p>Co-investigator Anushka Naidoo, B.Pharm, M Med Sc(Clin Pharm) CAPRISA eThekweni Research Site CAPRISA Research Pharmacy 3 Richards Rd, off Warwick Avenue Durban 4000 South Africa Tel Number: + 27 31 260 1963 Fax number: +27 31 3077 138 Email: naidooa2@ukzn.ac.za</p>
<p>Co-investigator Tanuja Gengiah, B.Pharm, M.Clin.Pharm 2nd Floor, Doris Duke Medical Research Institute Nelson R Mandela School of Medicine University of KwaZulu-Natal 719 Umbilo Road Congella 4013 South Africa Tel Number: +27 31 260 4262 Fax number: + 27 31 2604566 gengiaht1@ukzn.ac.za</p>	<p>Co-investigator Michele Upfold, B.Pharm CAPRISA Vulindlela Site CAPRISA Research Pharmacy University of KwaZulu-Natal 719 Umbilo Road Congella 4013 South Africa Tel Number: +27 33 260 6866 Fax number: + 27 31 2604566 upfold@ukzn.ac.za</p>

1. Background

In order to successfully test prevention interventions such as the 1% Tenofovir gel in the CAPRISA 004 study it is essential for users to adhere to the prescribed regimen and dosing instructions. Less than perfect adherence may reduce the test products' effectiveness and make results at the end of the study difficult to interpret, especially if the level of adherence is not assessed accurately (IOM 2008). The direct adherence assessment methods in microbicide trials rely heavily on participant self-report of gel use with a high associated dependency on participant recall. In these instances there have been published reports that participant self-report overestimates adherence when compared to more objective measures such as electronic drug monitoring (Berg and Arnsten 2006),(Simoni, Kurth et al. 2006). The limitations of self report include poor memory recall which differs by person, the need to give socially desirable responses as well as the time consuming nature of assisted recall (Pequegnat, Fishbein et al. 2000).

In the CAPRISA 004 study adherence is assessed by both direct and indirect measures. Direct measures include participant self report of gel use on last sex day prior to the clinic visit and number of gels used in the last 30 days. Indirect measures are obtained by pharmacy reconciliation of used and unused applicators returned by participants at each study visit. New innovations such as the Wisebag aim to support providers and participants by providing an indirect, objective measure of adherence that may be utilised to validate participant self report.

2. Pilot Study Purpose

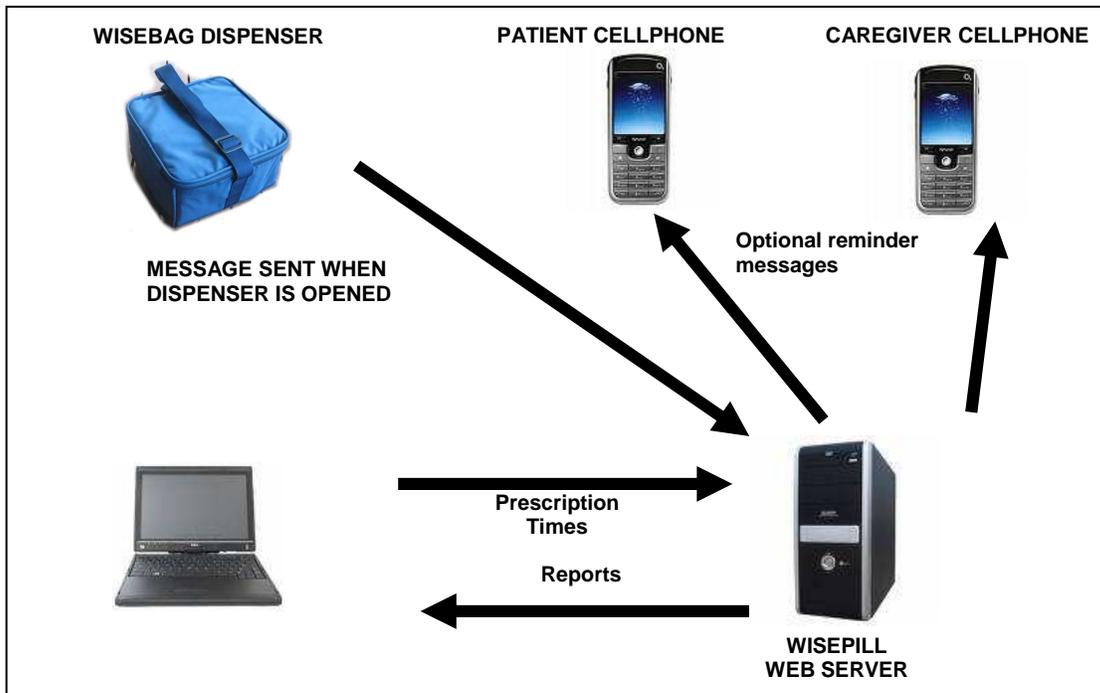
The purpose of this feasibility pilot study is to determine the utility of the data generated by Wisebag as an appropriate tool to correlate transmitted opening times at which Wisebag was opened to retrieve gel as a means to objectively

validate self reported gel use since the last study visit. The premise on which this pilot study operates is that the bag is opened for the sole purpose of gel retrieval for vaginal insertion.

3. Prototype Wisebag Description

The Wisebag dispenser is currently in a prototype form especially manufactured for this pilot study. The soft bag has a built in pocket which houses an electronic unit that senses when the bag is opened by means of a reed-switch in the electronic box and a magnet sewed into the lid of the bag. The unit transmits a signal using GPRS to a central Wisepill® server, every time the bag is opened. If there is no cell phone reception, the electronic unit will store the “opening events” and transmit them as soon as there is reception. The Wisepill unit switches off completely between openings and therefore has a considerable battery life of up to 3 months.

Figure 1: Wisebag Dispenser



The date and time of each “opening” event is recorded in the Wisepill® database and can be accessed in tabular or graphical format. Data can also be exported to a number of formats, including Microsoft Excel and PDF file format. Participant identification is restricted to the use of unique numerical participant identifiers. For participants who have agreed to receive a short message service (sms), each time the bag is opened a sms in English or Zulu will be sent to the participant’s cell phone and the text in English will read: "Hello, please remember to insert the gel as you were taught at the clinic. Also don't use more than two gels in 24 hrs. Thank you". The isiZulu version of the sms message will read as follows:"Sawubona. Sicela ukuba ukhumbule ukushutheka uketshezi/igel njengoba wawufundisiwe e-Clinic. Futhi ungasebenzisi uketshezi/igel olungaphezu kolubili esikhathini esingamahora angu 24. Siyabonga."

4. Study Timeline, Sample Size and Sites

4.1 Pilot Study Timeline

The feasibility assessment will be divided into two phases.

Phase I: Ten participants will use the Wisebag for four months, and if it is found to be feasible after month one, they will continue the use of the bag until the end of the trial)

Phase II: Forty participants will use the Wisebag for up to 8 months, from the time that the Wisebag is available to the end of the trial)

4.2 Sample size

The phase I sample size is 10 and the phase II sample size is 40. Total sample size is 50.

4.3 Study sites

In phase I of the feasibility study, 10 CAPRISA 004 participants will be selected to receive the Wisebag for a four month initial period. Four participants will be

selected from the eThekwini site and 6 participants will be selected from the Vulindlela site. Participants will be requested to house and retrieve their assigned study gel from the Wisebag. If at the end of month one, phase I shows that the Wisebag is acceptable to participants and useful in assessing gel use, the Wisebags will be rolled out in Phase II to 40 additional participants (12 in eThekwini and 28 in Vulindlela) who will be invited to use the bags up to the end of the trial.

At the end of the month 3 of phase I and II, the acceptability and usefulness of the Wisebag will be assessed again and women in this pilot study will be offered the option of continuing with the Wisebag until the end of the trial.

Questionnaires used at Months 1, 3 and at study exit are in Appendix II.

5. Participant Selection Process

For both phases of the pilot study, participants will be randomly selected by the study statistician to receive a bag based on their prior gel requirements. Only participants who use 20 or fewer applicators in the month may be selected to receive the bag due to prototype size constraints. Should selected participants be unwilling to receive the selected bag or receive reminder sms each time they open the bag to retrieve gel then this will be documented including reasons for refusal and the bag will be reassigned to the next selected willing participant.

Participants who agree to participate in this study will be required to sign an informed consent form (Appendix I).

6. Standardized messaging to participants:

Phase I and Phase II

- The Wisebags are the property of CAPRISA and are to be utilized during the next month and at all monthly study visits the bag must be returned to the pharmacy.

- The bags have been specially manufactured to enable CAPRISA to receive a message similar to an 'sms' every time the bag is opened. This message provides the date and time the bag was opened.
- Participants will receive a cellphone sms when the bag is opened to remind them to insert the gel both before and after sex.
- The bag must be utilized solely for the storage and retrieval of unused gel.
- Used gel must be placed in the opaque strip forms bags and should not be housed in the gel bag either for storage or when returning to the pharmacy.
- The bag must be re-zipped after retrieving the applicator.
- Only one applicator should be retrieved at a time.

7. Proposed future application for the Wisebag

The bag is intended to eventually have multiple functionality. It is intended to also act as a medication reminder by sending sms to participants when programmed opening events do not seem to have occurred. It can also send messages to participants if opening events exceed preset limits for safe dosing.

References:

- Berg, K. M. and J. H. Arnsten (2006). "Practical and conceptual challenges in measuring antiretroviral adherence." J Acquir Immune Defic Syndr **43 Suppl 1**: S79-87.
- IOM (2008). Methodological Challenges in Biomedical HIV Prevention Trials. S. W. G. Lagakos, A.R. Washington,DC: 270.
- Pequegnat, W., M. Fishbein, et al. (2000). "NIMH/APPC workgroup on behavioral and biological outcomes in HIV/STD prevention studies: a position statement." Sex Transm Dis **27**(3): 127-32.
- Simoni, J. M., A. E. Kurth, et al. (2006). "Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management." AIDS Behav **10**(3): 227-45.

Appendix 1

Wisebag Feasibility Study Informed Consent Form

CAPRISA 054

A pilot study to assess feasibility of utilizing a prototype Wisebag for enhancing measurement of gel use in CAPRISA 004

PRINCIPAL INVESTIGATORS:

Dr L E Mansoor
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013
Durban, South Africa
Phone: 031-260 4641
Email: mansoor@ukzn.ac.za

Introduction

You are being asked to volunteer in a pilot feasibility study named above. The purpose of this research is to find out if a specially designed bag used to store your study gel will assist the CAPRISA 004 study in obtaining more accurate information on gel use. A total of 50 participants will be asked to volunteer to help test the bag over a minimum period of two months but not more than eight months. All participants will still be required to return the bags to the pharmacy every month at the monthly study visit the same time the used and unused study applicators are returned.

Your participation is voluntary

It is important that you know the following:

- Your participation in this pilot study is entirely voluntary.
- You may decide not to take part or to withdraw from the pilot study at any time.
- Your continued participation in the CAPRISA 004 trial will not be affected if you decide not to participate or discontinue participation in this pilot study.
- Procedures related to this study will be incorporated into your scheduled monthly CAPRISA 004 study visits.
- There is no additional reimbursement for volunteering to participate in this study.

Procedures

If you agree to participate in this pilot study you will be provided a special study bag that only participants in this pilot study will receive. This bag has to be returned to CAPRISA every month when you come in for your monthly CAPRISA 004 study visit.

As a participant in this pilot study you will be required to do the following:

1. Store the unused gel you receive on a monthly basis in the special Wisebag.
2. Open the bag only when you want to use the gel.
3. Retrieve one gel only at a time and re-zip the bag directly after removing the gel.
4. Be willing to receive text messages sent to your cell phone reminding you about study gel insertion. The message will read "Hello, please remember to insert the gel as you were taught at the clinic. Also don't use more than two gels in 24 hrs. Thank you".

5. Answer a set of questions on receipt of the pilot study bag and when you return the bag at one month after using, 3 months after using and at the end of the pilot study. You may decline offering an answer to any question.
6. Possibly participate in a focus group discussion with other women who are also participating in this pilot study.
7. The Wisebag remains the property of CAPRISA and will be required to be returned at the end of the study

Costs and risks to you

There is no cost to you. The bag is provided free of charge and in addition to your CAPRISA 004 study product bag. Although there is unlikely to be any direct personal risk or harm to you if you participate in this pilot study, there is a possibility that carrying the bag and receiving a reminder sms in the presence of others (family, partner, friends) who are not aware of your study participation, may lead to situations where you could be discriminated against or harmed. You are the best person to judge your personal situation so please bear this possibility in mind when you are deciding whether to participate in this pilot study. If you experience any difficulties related to being in possession of the bag or receiving reminder sms's, please return as soon as possible to the study site and let study staff know so that we may assist you.

CONFIDENTIALITY

You will be identified by a unique code. Personal information from your records will not be released without your written permission. You will not be personally identified in any publication about this pilot study. However, your records may be reviewed by study regulatory authorities, study sponsors and study monitors.

PROBLEMS OR QUESTIONS

If you ever have any questions about your participation in this pilot study you should contact Dr LE Mansoor at 031 2604641

If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the United States of America +001-919-544-7040 ext. 295 (please note that time differences and international calling rates apply for calls to the USA).

SIGNATURE PAGE:

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, please sign your name below.

_____	_____	_____
Volunteer's name (print)	Volunteer's signature	Date
_____	_____	_____
Name of staff member who administered consent (print)	Staff member's signature	Date
_____	_____	_____
Witness' name (print)	Witness' signature	Date

Appendix 2: Acceptability Assessment Questionnaires

CAPRISA 054

A pilot study to assess feasibility of utilizing a prototype Wisebag for enhancing measurement of gel use in CAPRISA 004

V 1.0, 29 January 2009

Date: PID: Phase:
dd/mm/yy

Cell phone number:

Complete section A when the bag is first assigned:

Section A: Please tick the appropriate box (Choose only 1 answer):

1. *At first glance what is your opinion of the Wisebag appearance?*

- Like
- Dislike
- Neither like nor dislike

2. *How do you feel about others seeing you carrying this bag?*

- Very happy
- Happy
- Unhappy
- Extremely unhappy
- No opinion

3. *Which bag do you think you would prefer to carry the study gel in?*

- The CAPRISA black bag
- Your own bag
- This Wisebag
- No preference

4. *How do you feel about the bag sending us a sms when you open it?*

- Very happy
- Happy
- Unhappy
- Extremely unhappy
- No opinion

5. *How do you feel about us sending you a SMS as a reminder to use study gel every time you open the bag?*

Very happy

Happy

Unhappy

Extremely unhappy

No opinion

Thank you for your time

CAPRISA 054

**A pilot study to assess feasibility of utilizing a prototype Wisebag for enhancing measurement of gel use in CAPRISA 004
Version 1.0, 29 January 2009**

Date: Month:

PID: Cell phone number:

Complete Section B when the Wisebag is returned at month 1, month 3 and at study exit.

After using the Wisebag for the past one/three/eight months please rate the following:

1. What is your opinion of the Wisebag appearance?

- Like
- Dislike
- Neither like nor dislike

1.1 If 'like' is selected above please answer the following question. More than one response may be selected. What exactly do you like about the Wisebag?

- Colour
- Shape
- Zip
- Size of the bag
- Other

If other, please specify: _____

1.2 If 'dislike' is selected above please answer the following question. More than one response may be selected. What exactly do you dislike about the Wisebag?

- Colour
- Shape
- Zip
- Size of the bag
- Other

If other, please specify: _____

2. *How do you feel about others seeing you carrying this bag?*

- Very happy
- Happy
- Unhappy
- Extremely unhappy
- No opinion

If applicable why?

3. *Which bag do you prefer to carry the study gel?*

- The CAPRISA black bag
- Your own bag
- This Wisebag
- No preference

If applicable why?

4. *Describe your experiences in storing the bag at home?*

- I have no problems in storing it at home
- I am having problems in storing it at home sometimes
- I am having problems in storing it at home most of the time
- I am having problems in storing it at home all of the time
- No opinion/experience

If applicable, what problems are you experiencing?

5. *Did you ever use the bag to store anything else apart from your gel?*

- No
- Yes

If yes, complete what the items were:

6. Think back to the last time you took a study gel from the bag.

6.1 Any problems in accessing the bag from its storage place when you needed it?

No

Yes

If yes, what was the problem?

6. 2 Any problems in opening the bag?

No

Yes

If yes, what was the problem?

6.3 Any problems in closing the bag after use?

No

Yes

If yes, what was the problem?

6.4 How long after opening was the bag closed?

Immediately

After a few minutes

After a few hours

7. Did you ever forget to close the bag after taking out gel?

No

Yes

Can't remember

8. *Each time you opened the bag you received a sms from us. How helpful was our reminder sms in assisting you to remember to use the gel correctly?*

- Very helpful
- Somewhat helpful
- Of little help
- The reminder sms was of no help at all to me

Explain response?

Thank you for your time