Pennsylvania State University, College of Medicine, Department of Family and Community Medicine Research Division	
Official Study Title	HPV self-sampling among women at the PSH well-women appointments
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PennState

HRP-591 - Protocol for
Human Subject Research

Protocol Title:
HPV self-sampling among women at the PSH well-women appointments

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Important Instructions for Using This Protocol Template:
This template is provided to help investigators prepare a protocol that includes the necessary information needed by the IRB to determine whether a study meets all applicable criteria for approval.

1. **GENERAL INSTRUCTIONS:**
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2. **CATS IRB LIBRARY:**
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3. **PROTOCOL REVISIONS:**
   - When making revisions to this protocol as requested by the IRB, please follow the instructions outlined in the Study Submission Guide available in the Help Center in CATS IRB (http://irb.psu.edu) for using track changes.
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If you need help…	
University Park and other campuses: Office for Research Protections Human Research Protection Program The 330 Building, Suite 205 University Park, PA 16802-7014 Phone: 814-865-1775 Fax: 814-863-8699 Email: irb-orp@psu.edu	**College of Medicine and Penn State Health:** Human Subjects Protection Office 90 Hope Drive, Mail Code A115, P.O. Box 855 Hershey, PA 17033 (Physical Office Location: Academic Support Building Room 1140) Phone: 717-531-5687 Email: irb-hspo@psu.edu

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1.0 Objectives

1.1 Study Objectives

The main objective is to compare the test characteristics of the Human Papillomavirus (HPV) self-sampling kit versus clinician-sampled HPV testing for cervical cancer screening. This study seeks to find out if the HPV self-sampling kit is non-inferior to standard clinician-sampling practices.

1.2 Primary Study Endpoints

The primary outcomes of this study are to analyze the screening results on self-sampling kits compared to clinician-collected HPV test and Pap smear results.

1.3 Secondary Study Endpoints

Secondary endpoints will include acceptability of self-sampling and barriers to cervical cancer screening. These endpoints will be analyzed to try to circumvent barriers to the cervical cancer screening and ascertain whether self-sampling is a viable alternative.

2.0 Background

2.1 Scientific Background and Gaps

The American Cancer Society estimates that 4,170 women in the United States (US) will die from cervical cancer in 2018.[1] Screening can reduce cancer mortality by (1) detecting malignancies when they are more treatable[2] and (2) for some tests, identifying precancerous lesions for removal. Guidelines recommend cytology and/or human papillomavirus (HPV) testing for cervical cancer screening among women ages 30-65 years, but screening rates are suboptimal. [3, 4]

To help bridge these gaps in screening, HPV self-sampling would be an alternative to clinical screening. However, there are concerns about the efficacy and comparability of self-sampling kits as an effective tool to detect cervical cancer.

2.2 Previous Data

There have been previous studies about the effectiveness of self-collected samples as an alternative to clinician collected samples. Some studies state that HPV testing is more sensitive than Pap testing.[5] There is a possibility that these to samples have similar sensitivity.[6] Based on this information, examining test characteristics and acceptability of each technique is necessary to support larger efforts to make self-sampling available.

2.3 Study Rationale

The impact of the proposed project is to compare HPV self-screening results with Pap smear results, clinician-collected HPV test to ultimately improve the uptake of HPV screening. This study will be conducted in a normal risk population.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

1. Ages 30-65 years
2. PSH patient attending a well-woman visit (i.e., receiving an in-office cervical cancer screening) and able to collect the sample within the collection period (14 days before or 21 days after in-office cervical cancer screening).
3. Female
4. Has an intact cervix
5. Speaks, reads or writes well in English

3.2 Exclusion Criteria

1. Pregnancy
2. Cognitively impaired
3. Incarcerated
4. Complete hysterectomy
5. History of cervical treatment for abnormal Pap/HPV test (i.e., cryotherapy, Loop Electrosurgical Excision Procedure (LEEP))

3.3 Early Withdrawal of Subjects

3.3. 1 Criteria for removal from study

If the subjects does not complete the study activities they will be removed from the study. We don't anticipate clinician removal because study procedures are low risk.

3.3. 2 Follow-up for withdrawn subjects

The withdrawal will be documented and the subject will be replaced if the timeline allows

4.0 Recruitment Methods

4.1 Identification of subjects

A. Subjects will be identified in one of the following ways from participating Penn State Health clinics when they have a scheduled well-woman appointment:

(1) Clinicians on the study team will prospectively review their clinic schedules two weeks in advance and identify patients that could meet eligibility criteria for this study. They will send the contact information for these patients to study team members through a secure message in the Electronic Medical Record.

(2) Another member of the study team will prospectively review clinician schedules two weeks in advance and identify patients that would meet eligibility criteria for this study. Contact information for these patients will be entered directly into the REDCap database.

The REDCap database is used by study team members for participant tracking and data collection purposes. Separate data collection instruments for participant tracking and data collection will be used within the same REDCap project. Once recruitment is finished, the

contact information for individuals who declined participation or did not respond to recruitment attempts will be deleted.

(3) Clinicians will provide general information (via recruitment info cards and study flyers) about the study during the well-woman visit (if the patient was not previously contacted or was scheduled less than two weeks from their appointment). Patients will be advised to contact the study team using the information on the card/flyer if interested in participating. Study flyers will also be displayed publicly in clinic exam rooms.

Clinic staff who are not members of the study team will also be given recruitment materials, including information cards and study flyers. Non-study team members distributing recruitment materials will direct patients to the contact information provided on the information card and flyer.

(4) After a patient's appointment, if the clinician believes the individual could meet eligibility criteria for the study, the clinician will send the contact information for these patients to the study team members through a secure message in the Electronic Medical Record. For this fourth option, patients would not have been presented with the research opportunity during their appointment; clinicians may not have had a recruitment card available to give to their patient or may simply have forgotten to share the study opportunity. This option is only available for patients of IRB-approved study team members.

(5) Subjects will be identified from participating Penn State Health clinics if they are scheduled to receive a cervical cancer screening with a clinician on the study team. A report of potentially-eligible patients will be pulled from the Penn State Health electronic medical records twice per month via population health reports. Prior to their upcoming appointment, the study team will send a letter (study invitation letter) inviting the individual to participate in the study. A copy of the study flyer will also be included in the mailing. Individuals will be advised to contact the study team using the information on the letter if interested in participating. They will also be advised that they can discuss the research opportunity with their clinician at their upcoming appointment.

Before sending letters to their patients, all clinicians on the study team will be asked to provide permission for the study team to contact their patients. Permission will be given for all patients, not for each individual patient.

4.2 Recruitment process

4.2. 1 How potential subjects will be recruited.

197 subjects will be recruited to participate in the protocol. Clinicians will identify participants they think would be eligible for the study and either provide some general information (via the recruitment cards and study flyers) to the participants or provide their contact information to the study team members so that they may contact the participant themselves. Members of the study team (both clinicians and non-clinical staff) will prospectively review clinic schedules in order to help identify potential participants, and clinicians may also identify patients after their scheduled appointment. This will ensure that enrollment numbers are met and that all potentially eligible participants are provided with a recruitment card and/or study flyer by their clinician or contacted directly by a study team member.

4.2. 2 Where potential subjects will be recruited.

Participants will be recruited at their well-women appointment in the clinician's office or over the phone by a study team member.

4.2. 3 When potential subjects will be recruited.

Potential subjects will be recruited by a clinician at participating clinics when they have a well-woman appointment or are making a well-woman appointment. Participants whose contact information was provided to study team members by the clinician or collected by another member of the study team will be contacted 10-14 days prior to their well-woman appointment. Participants who are given a recruitment card and/or study flyer will contact the study team if they are interested in participating. Participants who are contacted by the study team after their appointment will be contacted within 1-2 days of receiving their contact information from the clinician via the EMR.

4.2. 4 Describe the eligibility screening process and indicate whether the screening process will occur before or after obtaining informed consent. Screening begins when the investigator obtains information about or from a prospective participant in order to determine their eligibility. In some studies, these procedures may not take place unless HIPAA Authorization is obtained OR a waiver of HIPAA Authorization when applicable for the screening procedures is approved by the IRB. [*For FDA regulated studies, consent for any screening activities would need to be obtained prior to screening unless specifically waived by the IRB.]*

Initial screening will occur before obtaining informed consent via their clinician/other study team member based on patients that are scheduled for upcoming appointments and that likely meet the inclusion criteria, or patients that are identified after their appointment and that likely meet the inclusion criteria. The clinician will then provide a study team member with the phone number of the potential participant, or this information will be entered directly into the REDCap database by a member of the study team. Also, at the well-woman appointment, the clinician may mention the study and give the subject a recruitment card with a study team member's contact information if they are interested. A study team member will complete the screening process and then obtain verbal implied consent over the phone. Then, a study team member will mail the participant the study materials and the summary explanation of research.

5.0 Consent Process and Documentation

5.1 Consent Process:

Check all applicable boxes below:

☐ **Informed consent will be sought and documented with a written consent form *[Complete Sections 5.2 and 5.6]***

☒ **Implied or verbal consent will be obtained – subjects will not sign a consent form (waiver of written documentation of consent) *[Complete Sections 5.2, 5.3 and 5.6]***

☐ **Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception). *[Complete section 5.2, 5.4 and 5.6]***

☐ **Informed consent will not be obtained – request to completely waive the informed consent requirement. *[Complete Section 5.5]***

The following checkbox is for all locations EXCEPT Penn State Health and College of Medicine:

☐ **Exempt Research at all Locations Except Penn State Health and the College of Medicine: If you believe that the research activities outlined meet one or more of the criteria outlined in "HRP-312- Worksheet- Exemption Determination." Please verify by checking this box that if conducting an exempt research study, the consent process will disclose the following (all of which are included in "HRP-590- Consent Guidance for Exempt Research"):**

Penn State affiliation; name and contact information for the researcher and advisor (if the researcher is a student); the activities involve research; the procedures to be performed; participation is voluntary; that there are adequate provisions to maintain the privacy interests of subjects and the confidentiality of the data; and subjects may choose not to answer specific questions.

If the research includes the use of student educational records include the following language in this section (otherwise delete): The parent or eligible student will provide a signed and dated written consent that discloses: the records that may be disclosed; the purpose of the disclosure; the party or class of parties to whom the disclosure may be made; if a parent or adult student requests, the school will provide him or her with a copy of the records disclosed; if the parent of a student who is not an adult so requests, the school will provide the student with a copy of the records disclosed.

Note: If this box has been checked, skip the remainder of section 5 and proceed to section 6 of this protocol. If the investigator's assessment is inaccurate, an IRB Analyst will request revision to the protocol and that an informed consent form be submitted for review and approval. Except for exemptions where Limited IRB Review (see "HRP-312- Worksheet- Exemption Determination") is required or where otherwise requested by the IRB, informed consent forms for research activities determined to be exempt without Limited IRB Review are generally not required to be submitted for review and approval by the University Park IRB.

5.2 Obtaining Informed Consent

5.2. 1 Timing and Location of Consent

Participants will be verbally consented for the initial screening up to 14 days before or 21 days after their well-woman appointment over the phone and answers will be input into REDCap by a study team member. Participants will receive a summary explanation of research mailed to their home with study materials.

5.2. 2 Coercion or Undue Influence during Consent

After a review of the research study via the Summary Explanation of Research, subjects will decide if they give consent to participate in the study. Subjects will be reminded that they may refuse to answer any question and end their participation at any time. At all stages of the recruitment and consent process, participants will be reminded that participation is voluntary and that they may withdraw without penalty at any time.

5.3 Waiver of Written Documentation of Consent

5.3. 1 Indicate which of the following conditions applies to this research:

☒ The research presents no more that minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

OR

☐ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. (*Note: This condition is not applicable for FDA-regulated research. If this category is chosen, include copies of a consent form and /or parental permission form for participants who want written documentation linking them to the research.)*

OR

☐ If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. (*Note: This condition is not applicable for FDA-regulated research.)*

Describe the alternative mechanism for documenting that informed consent was obtained:

Verbal implied consent

5.3. 2 Indicate what materials, if any, will be used to inform potential subjects about the research (e.g., a letter accompanying a questionnaire, verbal script, implied consent form, or summary explanation of the research)

Verbal script, summary explanation of the research, recruitment card, study flyers, study invitation letter.

5.4 Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception).

5.4. 1 Indicate the elements of informed consent to be omitted or altered

Not applicable.

5.4. 2 Indicate why the research could not practicably be carried out without the omission or alteration of consent elements

Not applicable.

5.4. 3 Describe why the research involves no more than minimal risk to subjects.

Not applicable.

5.4. 4 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable.

5.4. 5 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable.

5.4. 6 Debriefing

Not applicable.

5.5 Informed consent will not be obtained – request to completely waive the informed consent requirement

5.5. 1 Indicate why the research could not practicably be carried out without the waiver of consent

Not applicable.

5.5. 2 Describe why the research involves no more than minimal risk to subjects.

Not applicable.

5.5. 3 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable.

5.5. 4 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable.

5.5. 5 Additional pertinent information after participation

Not applicable.

5.6 Consent – Other Considerations

5.6. 1 Non-English-Speaking Subjects

We do not plan on soliciting non-English speaking or limited English speaking participants at this time. If unexpectedly encountered, a short from and oral translation process will be used to obtain informed consent. Our institution has translators available to assist.

5.6. 2 Cognitively Impaired Adults

5.6.2.1 Capability of Providing Consent

Not applicable.

5.6.2.2 Adults Unable to Consent

Not applicable.

5.6.2.3 Assent of Adults Unable to Consent

Not applicable.

5.6. 3 Subjects who are not yet adults (infants, children, teenagers)

5.6.3.1 Parental Permission

Not applicable.

5.6.3.2 Assent of subjects who are not yet adults

Not applicable.

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☐ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☒ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☒ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2. 1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2 .1.1 Plan to protect PHI from improper use or disclosure

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2 .1.2 Plan to destroy identifiers or a justification for retaining identifiers

Identifiers will be destroyed after the completion of data collection.

6.2. 2 Explanation for why the research could not practicably be conducted without access to and use of PHI

The proposed study requires enrollment of participants who are getting a clinical Pap/HPV test to compare those results with the findings from a self-sampled HPV test. Identification of these patients would be infeasible using other methods.

6.2. 3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

The waiver is necessary in order to screen participants for eligibility using the patient's medical record prior to their consent to participate in this study. This method will allow study team members to efficiently identify patients who are receiving/have received a Pap/HPV test. Many well-woman exams do not require a Pap/HPV test and it is not practical to provide information to all of these patients.

6.3 Waiver or alteration of authorization statements of agreement

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

After identification, a study team member will talk with potential participants over the phone to determine those that meet the study eligibility criteria. HPV self-sampling kits, with the summary explanation of research, will be mailed to study participants to complete within a week.

If a participant is contacted prior to their well-woman appointment: 3-5 days before the well-woman appointment, the research project manager will reach out to check if study participants have completed their HPV self-sampling kit. Those that have completed the kit will complete a survey over the phone and get an appointment reminder. They will mail their HPV self-sampling kit to the Penn State Health clinical lab. Those that have not completed their HPV self-sampling kit will get instructions to not use the HPV self-sampling kit before the well-woman and get an appointment reminder. They will be told they can complete the HPV self-sampling kit one week after their appointment. If the first self-sampling kit is lost or not received, we will mail a second self-sampling kit. They will then go to their appointment where the clinician will perform the Pap smear/HPV test. If the participant did not complete the self-sampling kit, two weeks after the well-woman appointment a study team member will schedule a time to call the participant to determine if she completed the HPV self-sampling kit and, if so, complete a survey over the phone. If the participant is not able to be reached or has not completed the HPV self-sampling kit, the study team will perform up to three follow up calls per participant. Once an HPV self-sampling kit has been completed and the analysis has been received from the Penn State Heath Clinical lab, study participants will be mailed their compensation within 1 week. Only one sample per participant will be mailed to the Penn State Heath Clinical lab where they will receive and analyze each sample. Analysis of the self-sampling specimens will be conducted to determine HPV DNA positivity to compare to results of the previous Pap/HPV test. In the unlikely event that not enough sample is collected, the participant will still be compensated for their efforts, and the study team will take note of how much sample was deemed too little for analysis and they will be excluded from data analysis. EMR data will be used to check insurance status, and the date and result of PAP/HPV tests

If a contacts the study team after their well-woman appointment: The patient will reach out to the research project manager to check eligibility. If eligible, the research project manager will send a kit and summary explanation of research and ask the patient to complete the kit within two weeks. Remaining procedures will be identical to the procedures for participants contacted prior to their well-woman appointment.

If a patient is contacted after their well-woman appointment: The study team will reach out to the patient to check eligibility. If eligible, the research project manager will send a kit and summary explanation of research and ask the participant to complete the kit within two weeks. Remaining procedures will be identical to the procedures for participants contacted prior to their well-woman appointment.

7.2 Study Procedures

Survey and HPV self-sampling kit

7.2. 1 10-14 days before/after the well-woman appointment

A study team member will obtain verbal consent from the participants to screen them for eligibility, and if they are eligible and agree to participate, a study team member will mail a self-sampling kit and summary explanation of research to be completed within 1 week.

7.2. 2 3-5 days before the Well-Woman appointment OR 13-21 days after Well-Woman appointment

Study physicians will perform the Pap smear/HPV test per standard clinical guidelines. Participants will complete the HPV self-sampling kit on their own time and mail it to the Penn State Heath Clinical lab in a pre-labeled package provided by the study team.

3-5 days before the Well-Woman appointment: A study team member will call study participants to provide a reminder to attend their well-woman appointment (if necessary) and take a survey over the phone if they completed their HPV self-sampling kit. Those that did not complete the HPV self-sampling kit will get an appointment reminder (if needed) and be told not to use the self-sampling kit until after the Well-Woman appointment. They will be told they can complete the HPV self-sampling kit a week after their appointment.

13-21 days after Well-Woman appointment: For participants who did not complete their HPV self-sampling kit before their well-woman appointment, a study team member will call study participants to ascertain if they completed their HPV self-sampling kit and take a survey over the phone. If they still have not completed it or could not be reached, the study team will contact them up to 3 more times to gather information. Although participants must collect their sample within 21 days of their well-woman appointment, participants may be called up to seven days past day 14 in order to account for weekends and holidays and to give participants time to return phone calls if necessary. Participants will not be contacted after day 21.

7.3 Duration of Participation

Participants will be in the study for up to five weeks.

7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

7.4. 1 Description

The Evalyn® Brush is a self-sampling kit that screens for HPV, a leading cause of cancer death among women. This tool has recently been FDA approved, but has not been incorporated into national clinical guidelines. This product is a small pink capped brush that can be used to take a sample of cervical cells.

7.4. 2 Treatment Regimen

Participants will take a sample of their cervical cells that amounts to a few milliliters of bio specimen.

7.4. 3 Method for Assigning Subject to Treatment Groups

Not applicable

7.4. 4 Subject Compliance Monitoring

Subject compliance will be confirmed once their lab results are received from the Penn State Heath Clinical lab.

7.4. 5 Blinding of the Test Article

Not applicable

7.4. 6 Receiving, Storage, Dispensing and Return

7.4 .6.1 Receipt of Test Article

1 HPV self-sampling kit will be sent to the Penn State Heath Clinical lab in a prepaid mailing. Inside the mailing will be the HPV self-sampling kit with the instructions and a Penn State Heath Clinical lab Pathology Services Special Account Requisition form. Kits will be purchased by the Department of Family and Community Medicine.

7.4 .6.2 Storage

Before HPV self-sampling kits are sent to study participants, they will be stored in a locked cabinet in the Department of Family and Community Medicine offices at 134 Sipe Ave. Kits mailed to the lab will be disposed of after analysis.

7.4 .6.3 Preparation and Dispensing

Before it is sent to the participant, the Penn State Heath Clinical lab Pathology Services Special Account Requisition document will be labeled with the participant's ID #, date of birth, and sex. The Mailing will include the HPV self-sampling kit with the instructions, a summary explanation of research, Penn State Heath Clinical lab Pathology Services Special Account Requisition form and Moss_Self-sampling Letter. Also, the package will include a prepaid and labeled mailing to send the kit and Pathology Services Special Account Requisition document to the Penn State Heath Clinical lab. Participants will need to include the date and time of sample collection on the Requisition form.

7.4 .6.4 Return or Destruction of the Test Article

The samples will be analyzed and the kits will be destroyed by the Penn State Heath Clinical lab once analysis is complete.

7.4 .6.5 Prior and Concomitant Therapy

Not applicable

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

197

8.2 Sample size determination

Assuming $p<.05$ and $beta>0.80$, we need 197 participants to determine concordance/non-inferiority of test results across the two different methods using a Fisher's exact test and Cohen's kappa coefficient.

8.3 Statistical methods

We will conduct Fisher's exact tests to examine our primary study outcome, i.e., concordance/non-inferiority of HPV self-sampling test results versus clinician-sampled test results. Additional analyses of the concordance across test will use Cohen's kappa coefficient. In addition, we will summarize survey

results using descriptive analysis, including calculating means, Pearson's correlation coefficients, and Fisher's exact tests.

9.0 Data and Safety Monitoring Plan

9.1 Periodic evaluation of data

Not applicable.

9.2 Data that are reviewed

Not applicable.

9.3 Method of collection of safety information

Not applicable.

9.4 Frequency of data collection

Not applicable.

9.5 Individuals reviewing the data

Not applicable.

9.6 Frequency of review of cumulative data

Not applicable.

9.7 Statistical tests

Not applicable.

9.8 Suspension of research

Not applicable.

10.0 Risks

Potential risks associated with this research are minimal. Loss of confidentiality is a risk of participation. All information entered into REDCap will be password protected with limited access to specific members of the study team. There may also be a risk of discomfort from participants misusing the self-sampling kit

11.0 Potential Benefits to Subjects and Others

11.1 Potential Benefits to Subjects

None

11.2 Potential Benefits to Others

Understanding how the results of the HPV self-sampling kit compare to clinician-collected HPV tests and Pap smears will ultimately help to create a better screening process. If the findings are similar across tests, HPV self-sampling may emerge as an effective option for cervical cancer screening among underserved populations without routine access to preventive healthcare.

12.0 Sharing Results with Subjects

Not applicable.

13.0 Subject Payment and/or Travel Reimbursements

Per institutional policy a Greenphire Clincard in the amount of $15 will be issued to each participant within one week of receipt of their self-sampling kit. A thank you card will be sent along with each Greenphire card.

14.0 Economic Burden to Subjects

14.1 Costs

Not applicable.

14.2 Compensation for research-related injury

Not applicable.

15.0 Resources Available

15.1 Facilities and locations

Participants will be recruited from Penn State Health Family and Community Medicine and Penn State Health Medical Group clinics. These clinics will be responsible for finding participants to recruit into the study. Participants will complete the HPV self-sampling kits on their own time and mail them to the Penn State Heath Clinical lab using a pre-labeled package provided by the study team. In addition, the study team member will collect survey data from participants through a phone survey.

15.2 Feasibility of recruiting the required number of subjects

Among the 10 study physicians and 1 CPN, at least 113 potentially-eligible patients receive a well-woman appointment each month. Based on their discernment, potentially-eligible patients will be invited to join the study, and they will be screened and consented if there are eligible. 790 subjects will be invited to join the study. Assuming that 25% of invited patients will agree to participate, it will take approximately 7 months to recruit 197 participants (~11 per month per provider).

15.3 PI Time devoted to conducting the research

The PI will use dedicated research time to conduct this research.

15.4 Availability of medical or psychological resources

Participants will all be patients at PSH HMC and will have access to the medical and psychological resources that are available to all patients.

15.5 Process for informing Study Team

The research team will meet regularly to discuss this study, its procedures, and any issues that may arise.

16.0 Other Approvals

16.1 Other Approvals from External Entities

Not applicable.

16.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – **Penn State** Health **only** – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of "HRP-902 - Human Tissue For Research Form" in CATS IRB.

☐ Animal Care and Use – **All campuses** – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – **All campuses** – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – **Penn State Health only** – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes but are no longer needed for clinical use. Upload a copy of "HRP-901 - Human Body Fluids for Research Form" in CATS IRB.

☐ Clinical Research Center (CRC) Advisory Committee – **All campuses** – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – **All campuses** – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – **Penn State Health only** – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of "HRP-903 - Radiation Review Form" in CATS IRB.

☐ IND/IDE Audit – **All campuses** – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – **Penn State Health only** – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Health Cancer Institute (PSCI) Protocol Review Committee or the PSCI Disease Team is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website.

17.0 Multi-Site Study

17.1 Other sites

Not applicable.

17.2 Communication Plans

Not applicable.

17.3 Data Submission and Security Plan

Not applicable.

17.4 Subject Enrollment

Not applicable.

17.5 Reporting of Adverse Events and New Information

Not applicable.

17.6 Audit and Monitoring Plans

Not applicable.

18.0 Adverse Event Reporting

18.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.0 Study Monitoring, Auditing and Inspecting

19.1 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

20.0 Future Undetermined Research: Data and Specimen Banking

20.1 Data and/or specimens being stored

Not Applicable.

20.2 Location of storage

Not Applicable.

20.3 Duration of storage

Not Applicable.

20.4 Access to data and/or specimens

Not Applicable.

20.5 Procedures to release data or specimens

Not Applicable.

20.6 Process for returning results

Not Applicable.

21.0 References

1. Siegel, RL, Miller, KD, Jemal, A. Cancer statistics, 2018. CA Cancer J Clin 2018;68(1):7-30.
2. Shieh, Y, Eklund, M, Sawaya, GF, et al. Population-based screening for cancer: hope and hype. Nature Reviews Clinical Oncology 2016.2.
3. U. S. Preventive Services Task Force. Final recommendation statement: Cervical cancer: Screening; 2018. https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/cervical-cancer-screening2. Accessed 2018.
4. Saslow, D, Solomon, D, Lawson, HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin 2012;62(3):147-172.
5. Mayrand, Marie-Helene, Duarte-Franco, Aliane, Rodrigues, Isabel, Walter, Stephen, Hanley, James, Ferenczy, Alex, Ratman, Sam, Coutlee, Franciis, Franco, Eduardo. Human Papillomavirus DNA versus Papanicolaou Screening Tests for Cervical Cancer. The New England Journal of Medicine
6. Polman, Nicole, Ebisch, Renee, Heideman, Danielle, Melchers, Willem, Bekkers, Ruud, Molijn, Anco, et al. Performance of human papillomavirus testing on self-collected versus clinician-collected samples for the detection of cervical intraepithelial neoplasia of grade 2 or worse: a randomised, paired screen-positive, non-inferiority trial. The Lancet Oncology's 2019, 20(2): 229-238.