Document Coversheet

Study Title: Pharmacokinetics, subjective effects, and abuse liability of nicotine salt-based vaping products with tobacco or unflavored e-liquids [SALTVAPE Study]

Institution/Site:	Roswell Park Comprehensive Cancer Center
Document (Approval/Update) Date:	09/07/2023
NCT Number:	NCT04231539
IRB Number	I 475819

ROSWELL PARK COMPREHENSIVE CANCER CENTER

Title: Pharmacokinetics, Subjective Effects, and Abuse Liability of Nicotine Salt-Based Vaping Products with Tobacco or Unflavored e-liquids [**SALTVAPE** Study]

Principal Investigator:
Amanda J Quisenberry PhD
Roswell Park Comprehensive Cancer Center
Elm and Carlton Streets
Buffalo, NY 14263
(716) 845-4918
Study Medical Doctor: Dr. Martin Mahoney
(716)845-3597

Roswell Park Study Number: I 475819

Consent Form Given to Participant Taking Part in an Investigational/Clinical Research Study

KEY INFORMATION ABOUT THIS RESEARCH STUDY

This is a clinical research study being done by the doctors at the Roswell Park Comprehensive Cancer Center and the University at Buffalo. Clinical research studies include only those participants who choose to take part. Your participation is voluntary. Please take your time to make your decision. Discuss it with your family and with people who are important to you.

We are asking you to take part in this study because there has been a dramatic increase in the use of nicotine base salt solutions due to the introduction of "Pods," the newest generation of Electronic Nicotine Delivery Systems (ENDS). Since nicotine base solutions are so new to the market, they have not been studied in detail. Therefore, we are interested in learning about ENDS users' perceptions and preferences towards inhaling vapors containing nicotine salt versus free-base nicotine.

Study Purpose: The purpose of this study is to determine and compare the levels of nicotine delivered to the bloodstream from nicotine salt and free-base nicotine e-liquid solutions. We will also assess and compare short-term nicotine effects of the different e-liquid solutions (e.g., nicotine cravings, withdrawal and satisfaction), puffing behaviors associated with the use of various e-liquid solutions, and users' perceptions and preferences towards the use of various e-liquid solutions.

Study Costs: The ENDS and e-liquid solutions that you will be using at each study visit will be provided to you at no cost.

Study Duration and Number of Participants: You will be asked to come in for 4 study visits, at least 5-7 days apart (with a maximum of 4 weeks between visits allowed before you are taken off

study). Each study visit is expected to last approximately 2.0 to 2.5 hours. The study will take about 4 years to complete.

Research Tests and Procedures:

- You will be asked to take 20 puffs over 10 minutes (one puff every 30 sec) from a vaping device we will provide you at the study visit.
- We will video record your study visit so that we can watch the video after the visit is complete and count the number of puffs you took during the puffing session.
- Certified trained phlebotomists or registered nurses will take blood samples from your arm and/or hand.
- Vital signs to measure your blood pressure, heart rate, and temperature and oxygen saturation will be measured.
- The level of carbon monoxide in your breath will be measured.
- Females of child-bearing age will be asked to provide a urine sample and be tested for pregnancy.
- You will be asked to provide a urine sample before and after product use so we may confirm your vaping status.
- You will fill out several questionnaires that will ask about your mood, any cravings you might be experiencing, how you liked the product that you tested, etc.
- In order to better understand how you use your vaping device, after all blood draws are completed you will be asked to puff on the assigned ENDS product as you normally would while a monitoring device called eTop is connected to take measurements.
- You will also use a Windows tablet to complete an Experimental Tobacco Marketplace task where you will be asked to pretend to purchase various tobacco products using a specified amount of money.

Section 3 of this document provides additional information on the tests and procedures involved with this study.

Side Effects and Risks: Overall, there is minimal risk for serious adverse reactions as a consequence of enrolling in this study.

Section 6 of this document provides more detailed information on possible side effects and risks.

Potential Benefits: There is no direct benefit for those who decide to participate and enroll in this study. You will be paid for your participation in this study as outlined in Section 11.

The type of study, the risks, benefits, discomforts, and other important information about this study are discussed below.

ADDITIONAL INFORMATION ABOUT THIS RESEARCH STUDY

It is important that you read and understand the following facts that apply to anyone that takes part in our studies:

a) This study is considered research. It is investigational.
b) Taking part in the study is voluntary.
c) You may withdraw from the study at any time without penalty, loss of any benefits or access to care at Roswell Park to which you are otherwise entitled.
d) Personal benefit may not result from taking part in the study, but knowledge may be gained that will benefit others.
e) If we become aware of important new information that may relate to your willingness to participate in this study we will inform you of this new information.
f) If we become aware of important new findings that relate to your participation or continued participation in this study we will discuss them with you.

1. What is the purpose of this study?

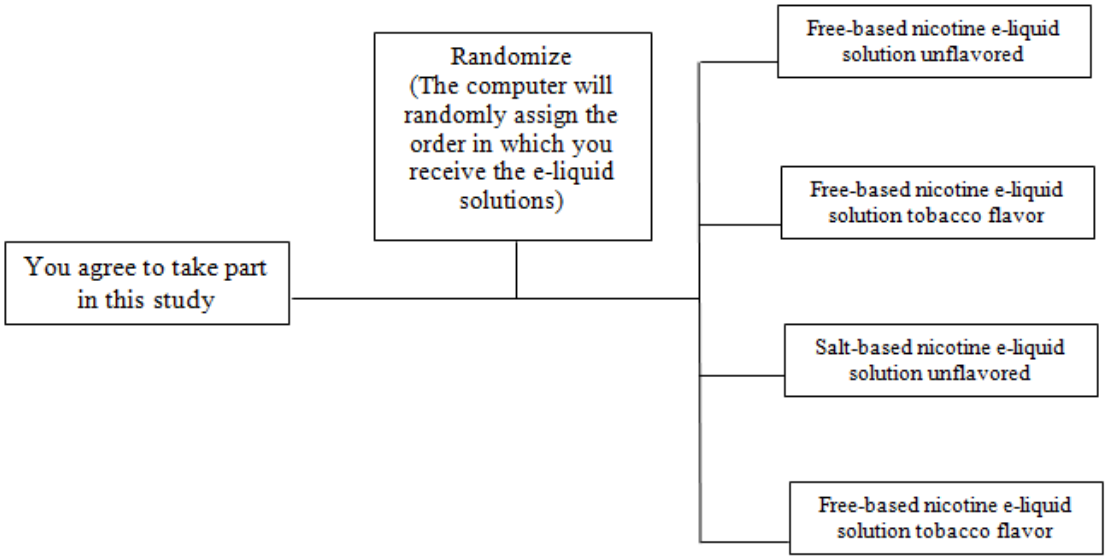
The purpose of this study is to determine and compare the levels of nicotine delivered to the bloodstream from nicotine salt and free-base nicotine e-liquid solutions. We will also assess and compare short-term nicotine effects of the different e-liquid solutions (e.g., nicotine cravings, withdrawal and satisfaction), puffing behaviors associated with the use of various e-liquid solutions, and users' perceptions and preferences towards the use of various e-liquid solutions.

2. What are the study groups?

During each visit, following an overnight abstinence, participants will be asked to take 20 puffs over 10 minutes (one puff every 30 seconds) from an assigned vaporizer (Innokin EQs Ultra-Compact 2ml Refillable Pod). Study personnel will set the device to 11.5W for every study session. The device will be filled with either (1) Unflavored free-based nicotine e-liquid solution (2) free-based nicotine e-liquid solution of tobacco flavor (3) Unflavored salt-based nicotine e-liquid solution or (4) salt-based nicotine e-liquid solution of tobacco flavor. Both the study personnel and study participants will be blinded to the solution flavor and nicotine concentration. All e-liquids will contain 0.148M nicotine (24 mg/mL free-base nicotine or 24 mg/mL nicotine benzoate).

A computer will by chance assign you to the order in which you receive the 4 different e-liquid solutions. This is called randomization.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines.



3. If I take part in this study, what tests and procedures will I have done?

You will be seen on 4 separate occasions, at least 5-7 days apart at Roswell Park (with a maximum of 4 weeks between visits allowed before you are taken off study). Each study visit is expected to last approximately 2.0 to 2.5 hours.

Before you come in for each study session, we ask that you refrain from using your vaping device and/or any other nicotine containing product. We will confirm that you have not smoked any tobacco product by a simple breath test that will measure the level of carbon monoxide in your breath. If the breath test reveals a high CO level, then we will assume that you have smoked a nicotine product and you will not be able to partake in the study session at that time.

During each study session, you will be asked to take 20 puffs over 10 minutes (one puff every 30 sec) from a product vaping device we will provide at each study visit (Innokin EQs Ultra-Compact 2ml Refillable Pod Vaporizer equipped with an 800mAh battery and wattage set to 11.5W). The vaping device you will be using is pictured below. You will be video-recorded at every session so that we can analyze your puffing behaviors (product operation, number of puffs, and time of puffing and exhaling vapors).

In addition, at every session, blood samples, to measure nicotine, will be taken by certified trained phlebotomists through a butterfly needle or through a venous catheter placed by a registered nurse before and 2, 4, 5, 6, 8, 10, 13, 15, 20, 30, 45, 60, 90, and 120 min after your puffing session with the vaping device. A total of 60 mL of blood may be collected using a 4mL green top heparinized vacutainer blood collection tube during each visit (15 collection time points, 4 mL at each time point, not all collection time points will be fulfilled at each visit). Because the butterfly needles are very small in size, if you experience excessive blood clotting and the blood is no longer flowing

from the needle, the butterfly needle will be removed and a new butterfly needle will be inserted to continue with blood collection (the number of new butterfly needle insertions will never exceed three per study session). The butterfly needle or venous catheter may be placed in your arm or the hand. Vital signs will be taken at the beginning of every session to measure your blood pressure, heart rate, temperature, and oxygen saturation. We will also use the CO breath test to measure the level of carbon monoxide in your breath before and 3 minutes after the use of the vaping device. Females of child-bearing potential will be given a urine pregnancy test at every study session.

At each study session, you will be asked to answer various questionnaires including: Demographics, Smoking History, Time-line Follow Back to assess past 30 day tobacco product use, Penn State E-cigarette Dependence Index, Taste Preference, Minnesota Nicotine Withdrawal Scale (MNWS), Positive and Negative Affect Scale (PANAS), Modified Questionnaire of Smoking Urges (QSU-brief), Drug Effect Questionnaire (DEQ-5), Sensory Measures, and Satisfaction with and Helpfulness of the Products. On the final session, visit 4, you will fill out a Product Satisfaction Scale rating each e-liquid you tested. Refer to Schedule of Procedures and Observations Table below for frequency of tests and procedures.

Additionally, you will be asked to complete the Experimental Tobacco Marketplace product purchasing task. During the ETM, you will purchase pretend tobacco products in an online store with an account balance determined by past 30 day-tobacco product use at Session 1. The vaping device sampled during your study visit will be available for purchase under four different price conditions. Other tobacco products will also be available at a constant price.

* presumed equivalent in nicotine yield to a single cigarette (based on pilot studies 20 puffs generate aerosol with cumulative nicotine yields from 1.5 mg to 1.7 mg)

Schedule of Procedures and Observations

Visit	#1	#2	#3	#4
Week	1	2	3	4
Nicotine Solution (randomized order)	E-liquid Solution #1	E-liquid Solution #2	E-liquid Solution #3	E-liquid Solution #4
Informed Consent[1]	X			
Questionnaires: Demographics and Smoking history, Time-line Follow Back, Penn State E-Cigarette Dependence Index, ENDS Nicotine Dependence Scale Taste Preference	X			
Vital signs	X	X	X	X
Blood Draw for Analytical Testing	X	X	X	X
Urine Pregnancy Test	X	X	X	X
Urine Sample (before and after 10min puffing session)	X	X	X	X
Puffing Topography	X	X	X	X
CO breath test *Pre and Post-Product Use*[2]	X	X	X	X
Questionnaire: Minnesota Nicotine Withdrawal Scale (MNWS)(adapted) *Pre and Post Product Use*	X	X	X	X
Questionnaire: Positive Negative Affect Scale (PANAS) *Pre and Post Product Use*	X	X	X	X
Questionnaire: Satisfaction With and Helpfulness of the Products *Post Product Use*	X	X	X	X
Questionnaire: Drug Effect Questionnaire (DEQ-5) *Post Product Use*	X	X	X	X
Questionnaire: Modified Questionnaire of Smoking Urges (QSU-brief) *Post Product Use*	X	X	X	X
Adverse Events	X	X	X	X
Concomitant Medications	X	X	X	X
Questionnaire: Product Satisfaction Scale *Post Product Use*				X
Experimental Tobacco Marketplace (ETM)	X	X	X	X
Questionnaire: Sensory Measures *Post Product Use & Delay Discounting Task*	X	X	X	X

1 Must be signed prior to any study related assessments or procedures.

2 Expired CO will be measured before, and 3 minutes after the use of each product

4. Will I be informed of research results?

If we learn new information from research tests or analyses during this study that may be important to your health or to your disease or condition, we will not be able to share that information with you because analysis may not be done until after the study is completed.

5. Why would I be taken off the study early?

You may be taken off the study for any of the following reasons:

- Any side effect from using ENDS; related or unrelated to intervention.
- The Investigator may discontinue a participant if, in his/her judgement, it is in the best interest of the participant to do so.

- Noncompliance (defined as missing scheduled visit by more than 2 weeks without contact).
- Participant voluntary withdrawal. A participant may withdraw from the study at any time, for any reason.

6. What risks and discomforts are involved?

- *Nicotine overdose:* Some people who use ENDS may experience symptoms of nicotine overdose such as nausea, sleep disturbance, headache, and vomiting; however, these symptoms are usually mild and temporary.
    - The PK studies using ENDS in participants will be performed in a clinical setting accustomed to monitoring for adverse effects. The Investigators have considerable experience with conducting outpatient studies on novel nicotine delivery devices and their effects on participants and will be able to provide appropriate safety monitoring.
    - Participants will also be instructed that the vaping products are not to be ingested. If a product is ingested by mistake, study personnel will contact the study physician (Dr. Mahoney - (716) 845-3597).
- *Nicotine withdrawal:* Many individuals who quit smoking exhibit a pattern of symptoms related to withdrawal from tobacco use. These symptoms include: sadness and anxiety, irritability, anger, difficulty concentrating, appetite change and weight gain, insomnia, and decreased heart rate. Because participants in the studies will be asked to refrain from smoking and/or using their ENDS for portions of the study, it is likely that they will experience some of these symptoms.
- *Respiratory irritation*: Some people who use ENDS may experience irritation of the airway of the upper respiratory tract, but as they are already regular ENDS users we do not think that this is likely.
- *Blood Draw:* is required for study participation and this could lead to local pain, swelling, bruising or infection. Significant complications (beyond typical local pain and mild bruising) are expected to be uncommon. *The volume of blood to be withdrawn will never exceed 60 mL on any planned visit*. This amount of blood is safe for the participants and will not produce any injury to a healthy individual.
- *Emotional distress:* Participants may experience psychological discomfort during assessments when discussing feelings and attitudes about smoking and using ENDS, or from learning about the risks of smoking. However, all participants will be current ENDS users and we do not expect this type of reaction to be likely. Study personnel will be alerted to expect this from a small number of participants and will be trained to make referrals for mental health services as needed. Personnel will be trained to query for adverse emotional reactions during assessments and will be trained to deal with such reactions and to provide additional referrals if needed. In addition, if assessments indicate psychiatric concerns, referrals to appropriate psychological services will be provided.

7. Reproductive risks:

Women will be advised to notify the study staff if they become or intend to become pregnant during the study period. Because nicotine and e-cigarette vapor safety for an unborn baby is

unknown, you should not use these products during pregnancy. Participants will be told that they should not become pregnant while on this study nor should they nurse a baby. If a woman is pregnant or breast feeding, she may not participate in this study, and if she becomes pregnant during the study, she will be removed from the study.

8. What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Abstain from using your ENDS device and/or any other nicotine product 8-10 hours before coming in for each study session.
- Tell study staff about:
  - All medications and supplements you are taking
  - Any side effects
  - Any changes in your ENDS use (i.e. if you stop vaping)
  - If you start smoking cigarettes

9. What will this cost?

You will be responsible for transportation to and from the research site and any costs that might entail. The ENDS and e-liquid solutions that you will be using at each study visit will be provided to you at no cost by the study sponsor. The remainder of the study will be conducted at no financial cost or obligation to you.

10. What happens if I am injured as a result of this study?

If you believe you have been injured as a direct result of your participation in this research study, notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor (Dr. Martin Mahoney) at (716) 845-3597.

Medical diagnosis and treatment for the injury will be offered, and a determination will be made regarding appropriate billing for the diagnosis and treatment of the injury. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

You do not give up any legal rights by signing this form. You are not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

11. Will I be paid for joining this study?

You will be compensated by cash for each study visit completed, and you will receive additional "bonus" cash if all study visits have been completed. Payments will be disbursed according to the following schedule:

Study Payment Schedule

Study Visit	Payment Amount
1	$50.00
2	$60.00
3	$70.00
4	$80.00
All Visits Completed	$90.00 bonus
TOTAL	$350.00

It is possible that this research project may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit by the sponsor or other entities. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your information and biospecimens (such as blood or tissue samples) collected as part of this research.

12. Where can I find more information?

You may call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

For accurate cancer information including Physician Data Query (PDQ), visit https://www.cancer.gov.

13. Who do I contact with questions?

You are free to ask questions at any time about this study and to ask for more information from the doctor identified on this document. If you have any questions, concerns or complaints about this study, you should contact the study doctor identified on the first page of this document.

If you have questions about your rights as a research participant or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Patient Advocate (Support) Office at (716) 845-1365. You should also feel free to contact the Patient Advocate Office at any time while considering participation, during participation or once your participation is complete. This office is unaffiliated with any specific research study. They can help you obtain additional information regarding your research participation and your rights as a research participant or how to proceed should you feel you have been injured as a result of your participation. They are available to discuss any problems, concerns, questions or input you may have.

It may be necessary to contact you at a future date regarding new information about the ENDS device or e-liquids that you tested. For this reason, we ask that you notify the study staff to update us of any change in your address.

CONFIDENTIALITY AND USE OF HEALTH INFORMATION

Your privacy is very important to us and the researchers will make every effort to protect it. Your information collected in this study may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect the study records and your information. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

• The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
• The Food and Drug Administration and the National Institutes of Health in the U.S.

Information that identifies you may be removed from your health information and/or biospecimens (such as blood or tissue samples, if applicable). The de-identified health information or biospecimens may then be used or disclosed for other purposes, including for future research studies or distributed to another investigator for future research studies, without additional informed consent or authorization from you or your legally authorized representative.

Certificate of Confidentiality

As an additional measure to protect your privacy, a Certificate of Confidentiality has been issued from the United States Government, National Institutes of Health, for this study. With this Certificate, the investigators and institutions involved in this study cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. We will use this Certificate to resist any demands for information that would identify you, with the following exceptions:

- The Certificate cannot be used to resist a request for your information from the United States Government when the information is to be used for auditing or evaluation of federally funded projects or for information that must be disclosed to meet the requirements of the Food and Drug Administration (FDA).
- State law requires we report cases of diseases that spread easily, or abusive behavior (toward a child, a partner, or an elderly person), and people who say they are going to hurt themselves or someone else.
- The Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or involvement in this research. Also, if you have given written consent to an insurer, employer, or other person to receive research information, then we may not use the Certificate to withhold the information.

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number to maintain confidentiality. All records will be kept in a limited access environment. Information will not be released without written authorization.

All analyses are completed as a group. No one individual participant's data will be used.

OPTIONAL RESEARCH

If there are still remaining amounts of your provided blood or urine, we would like to keep them for future research with your permission. If you agree, these samples will be kept in a specimen bank here at Roswell Park Comprehensive Cancer Center. These stored samples might be used for other research and might include genetic studies or diseases that are common to your age group.

If genetic testing is done, the sample will be labeled so your name and your identity will remain unknown to the researchers. The results of any genetic or other testing will not be given to you or your doctor, as your identity will not be known. It is not possible for us to know now what tests will be discovered in the future. We cannot give you a list of all the possible ways the sample will be used. We are asking that you give your permission for us to take, store and do research on the sample without contacting you again in the future. None of this research is a direct help to you, but it could help us learn other ways to prevent cancer or other diseases and might be helpful to others in the future. It is possible that future research projects may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your biospecimens (such as blood or tissue samples) that had been stored for future research.

These stored samples will be used for future research studies that may involve genetic or genomic studies and looking for links between genes and factors like diet or lifestyle, other cancers, or other diseases that are common in your age group. Body tissues are made up of cells that contain DNA (deoxyribonuclease acid), which is your unique genetic material that carries instructions on how your body develops and functions. Genetic studies look at certain genes (small segments of the DNA) and genomic studies, which may include whole genome sequencing, looks at the complete set or large segments of the DNA and how it may be changed or is different for people with diseases and those without. Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives.

You will receive no payment for these samples or from any, tests or products that are developed in the future from the use of the samples. If you give permission for the sample now and change your mind later, you will need to write to the investigator listed on the last page of this form and let him know that you changed your mind. The sample will then be destroyed and not used. If you have any questions, please ask your study staff.

Consenting to have your remaining samples stored in a tissue bank is not needed to take part in the rest of the study. If you decide not to join in this part of the study, you can still join the rest of the study. Any amounts remaining from the samples provided after running all specified study analyses, will be destroyed and tested no further.

1. Any remaining amounts of my provided blood or urine can be taken and kept for future research.

PLEASE CHECK ONE BOX

YES ☐ **NO** ☐

2**.** I agree that someone from Roswell Park Comprehensive Cancer Center may contact me in the future to ask me to take part in more research.

PLEASE CHECK ONE BOX

YES ☐ **NO** ☐

Statement of Investigator/Person Conducting the Informed Consent Discussion:

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained and that any questions about this information have been answered. A signed copy of this consent will be given to the participant.

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Participant's Statement of Consent:

By signing below, you agree that:

- You have been told of the reasons for this study.
- You have had the study explained to you.
- You have had all of your questions answered, including those about areas you did not understand, to your satisfaction.
- You have carefully read this consent form and will receive a signed copy of this form.
- You do **not** waive any **legal** rights you have under federal or state laws and regulations.
- You willingly give your consent to voluntarily join in this research study.

Participant:

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Witness Signature is needed in the following circumstances – check below:

☐ Not Applicable
☐ The person consenting cannot write – mark must be made as appropriate.
☐ The person consenting cannot read - consent has been read to him/her.
☐ The person consenting cannot understand English and the consent has been verbally interpreted.

(The witness should be fluent in both English and the language of the person consenting.)

Witness Statement:

The person consenting has signed this document in my presence.

SIGNATURE_____**DATE**_____ **TIME**_____

PRINTED NAME _____

RELATIONSHIP TO PARTICIPANT_____