OPERATIONS MANUAL

DATA COLLECTIONS WITH STUDY QUESTIONNAIRES

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Eric Lucas (lucas@iarc.fr) V 3

International Agency for Research on Cancer
Centre International de Recherche sur le Cancer

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CONTENTS

1. Introduction

This project is a multi-centric trial, so it is very important to have common logistics in each site:

- Same protocol;
- Same questionnaires;
- Same data collection process;
- Same information system (IS);
- Same logistics management;
- Same clinical procedures;
- Same quality control measures.

The purpose of this operations manual is to create processes and systems that result in research data being:

- Accurate;
- Complete;
- Timely;
- Verifiable;
- Secure;
- Available for analysis.

A. General interviewer tips:

- Help the participants to feel comfortable. Develop a reassuring relationship with them.
- Avoid re-phrasing items on the questionnaire, as doing so can change the meaning and could cause inconsistence with other interviews.
- Use probes to help the participant remember an answer, clarify a response, or to help report something more accurately.
- When a participant's response does not match one of the listed response categories, record the participant verbatim (word-for-word) and ask them the same question in another way to ensure you receive a proper reply.

It is important for you to review the forms for accuracy and completeness once the interview is complete. By reviewing the form briefly while the participant is still there, you can go back to an item that may have accidentally been skipped.
Ensure that there are no blank fields (NA if not applicable). Some forms require the information collected previously to be repeated such as name, address, etc and at such instances countercheck the information collected previously so as to avoid discrepancies.
While noting the height, at each vaccination, please note that there could be increase in height but it cannot decrease from the previous records.

B. 2 doses vs 3 doses data collection:

Some questionnaires contain data that we will collect only for specific groups (e.g. sero-testing group or 2 doses group or 3 doses group).
In general, the optional columns have a yellow background, so only collect data in these columns/fields when appropriate.

First example:

This part to be filled only if the participant is eligible

C. Participant's history		Day 1	Day 60	Day 180
1	Visit date: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
2	Age at menarche *in years*: *(77: not applicable; 99: if not known)*	☐☐	☐☐	☐☐
3	Date of last menstruation period: *(if applicable)*	__/__/20__	__/__/20__	__/__/20__
4	Age at marriage *in years*: *("77" if not applicable)*	⊘	☐☐	☐☐
5	Contraceptive method: *(1: none; 2: condom; 3: pill; 4: abstinence; 5: not applicable; 8: other (specify:); 9: not known)*	⊘	☐	☐
6	Comment:			
7	Staff Id:	☐☐	☐☐	☐☐
Data entry done:		○	○	○

If no update in questions 3-5 do not fill in the form

The 2nd column should not be used for the 2 doses group.

Second example:

F. Blood collection: (only for sero-testing group)		Day 1
1	Specimen collected: *(1: no; 2: yes)*	☐
2	Reason not collected: *(1: technical difficulty; 2: refused; 3: missing; 8: other reason (specify:))*	☐
3	Date specimen collected: *(dd/mm/yyyy)*	__/__/20__
4	Staff Id in the field clinic:	☐☐
Data entry done:		○

This table should only used if the patient is in the sero-testing group (15% of participants).
If not, leave this table empty.

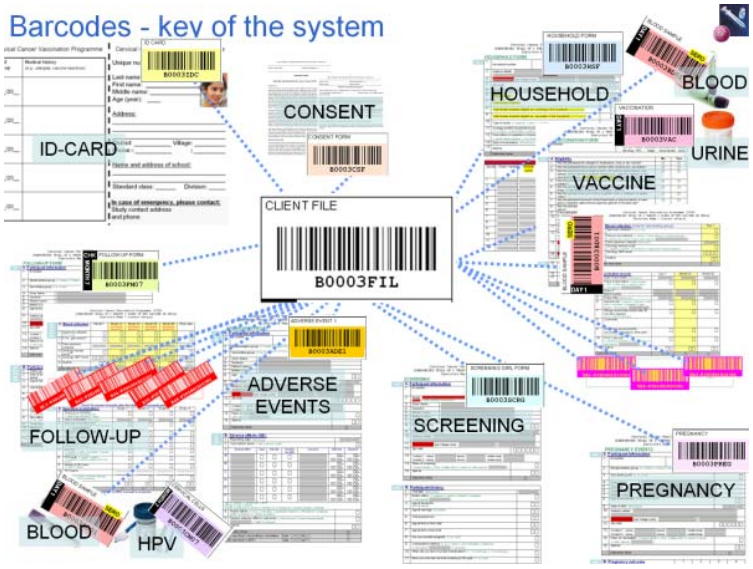
C. Questionnaire heading:

C.1 Unique number:

According to the different sites, the identification number will be compounded with different data: Study site, Group, primary health center (PHC) or panchayath, village number, house number (defined after the field enumeration) and the participant's individual number.

Site:	Ambillikai (A), Barshi (B), Delhi (D), Gujarat (G), Hyderabad (H), Mizoram (Z), Mumbai (M), Pune (P), Sikkim (S)
Group:	2 doses / 3 doses
PHC:	Primary health center code
Village:	Village code
House number:	House number according to house enumeration
Individual number:	Individual sequential number from each house according to house enumeration

C.2 Barcodes:



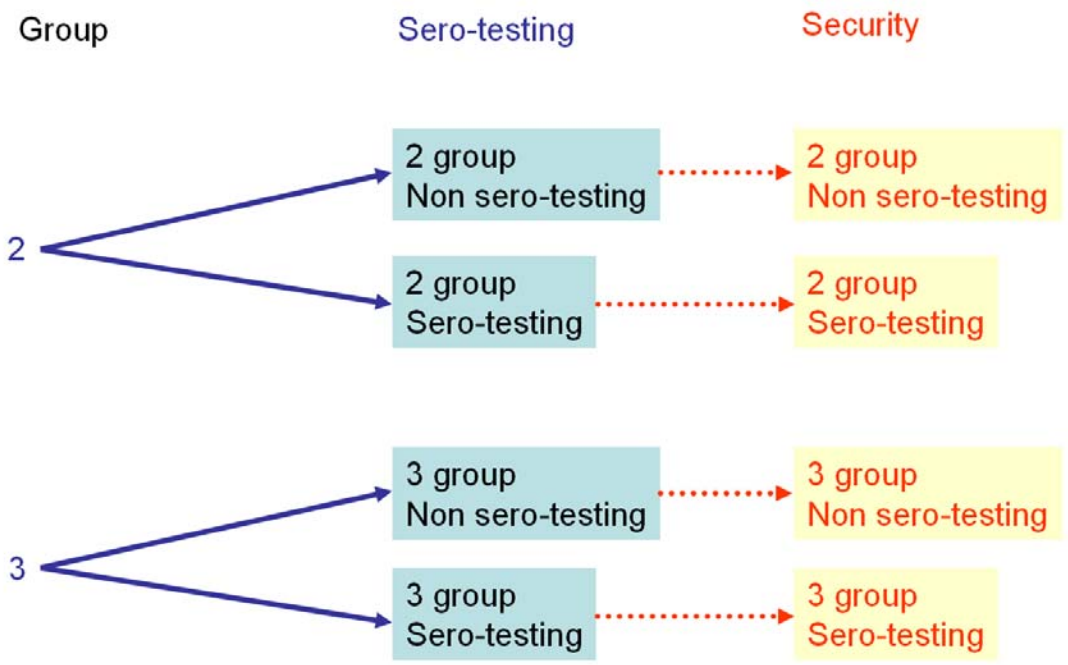
Barcodes are series of vertical lines and spaces that a scanner converts into an electrical signal understood by a computer. Barcodes can store alpha and numeric information and provide accurate, fast, real-time data collection and entry (especially for Id numbers). Barcode technology also offers an excellent security and minimizes possible errors associated with manual data entry.

C.2.a Barcode sheet:

A barcode sheet will be allocated for each eligible participant **the first day of the vaccination**. Each barcode number will be unique and should be used only for one specific participant during the entire project time.
The top part of the barcode sheet contains the title (Site name and type of barcode sheet), the questionnaire barcodes and the cryo specimen barcodes.

C.2.b Barcode sheet type:

We define 8 types of barcodes sheets depending on the participant group:



List of the barcode sheets type:

- 2 doses
- 2 doses / security
- 2 doses / sero-testing group
- 2 doses / sero-testing group / security
- 3 doses
- 3 doses / security
- 3 doses / sero-testing group
- 3 doses / sero-testing group / security

These groups were defined to allow to generate in advance for each study site the appropriate number of barcode sheets. The security barcode sheets correspond to an extra 5% of security stickers for each category.

Remark:
The questionnaire barcodes will be exactly the same for all the sheet types, but the cryo specimen barcodes will differ depending on the sero-testing group type. For the non-sero testing group we will have less barcodes.

VACCINATION

Barcode format

To simplify field logistics, the unique number and barcode number will not be the same: Barcode number will also be a compounded number with one letter for the site (e.g. "B" for Barshi) + 4 digits for the serial number (e.g. "0001" to "4000") + a string of 3 or 4 characters to determine one action (e.g. vaccination).
Each participant at the time of the vaccination will receive a study number (e.g. B0003) and a barcode sheet that the project team will use to identify questionnaires and specimens during all the length of the study.

Each barcode sheet will be directly generated by IARC and distributed to the sites. They should be used only for a specific participant and under no circumstances should a barcode be allocated to another participant to avoid protocol violation.

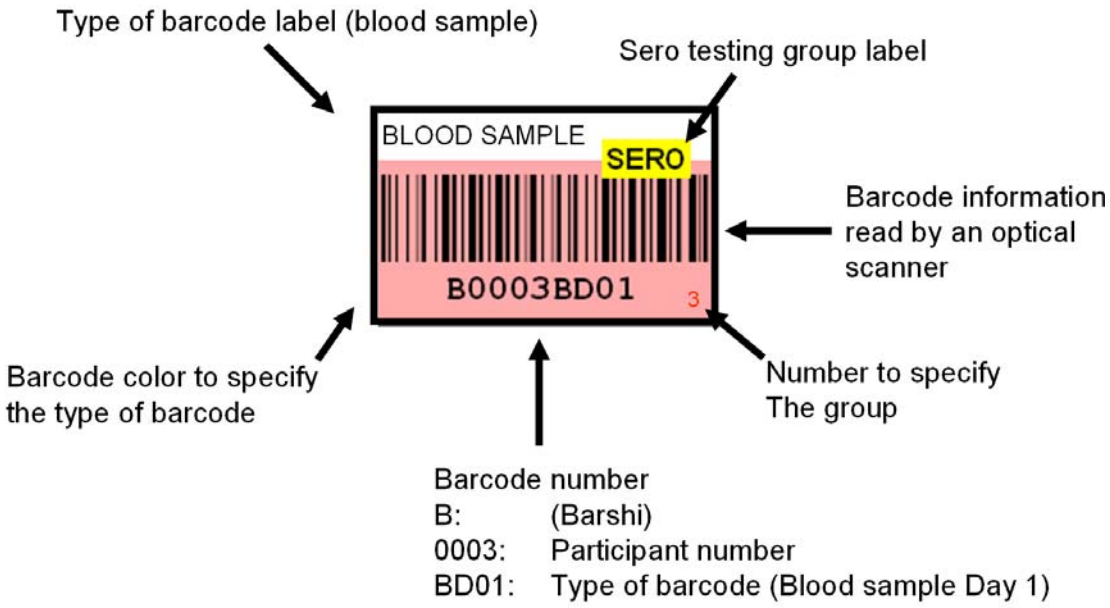
A barcode is defined by the site, serial number and the type of barcode (string).
Each barcode will also have a colour to facilitate its use.

Sero-testing groups will be identified by a yellow message "SERO" on the top of the barcode.

If barcodes sheets are missing or if you need more, please to contact IARC to receive more sheets.

In case of error with the use of barcodes please inform IARC as soon as possible.

C.2.c Questionnaire barcode presentation:

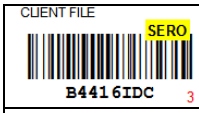
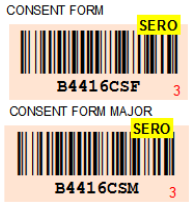


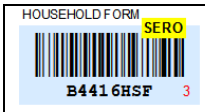
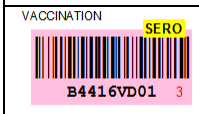
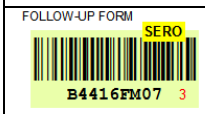
C.2.d Questionnaire barcode colors and code dictionaries:

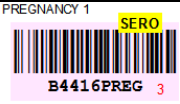
Color	Type of barcode	Code
	Client file	IDC
	Consent form signed by parents Consent form major	CSF CSM
	ID Card	IDC
	Household form	HSF
	Vaccination form Vaccination (injection)	VD01 (Day 1)
	Follow-up form	FM07 (Month 7)
	Acceptability form	ACCF
	Update/discontinuation	UPD
	Adverse event	ADE1 (N°1)/ ADE2 (N°2) ADE3 (N°3)/ ADE4 (N°4) / ADE5 (N°5)
	Screening girl	SCRG
	Screening mother	SCRM
	Pregnancy participating girl	PREG

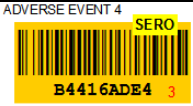
C.2.e Barcode legends

Based on the barcode sheet for a 3 doses and sero-testing groups participant

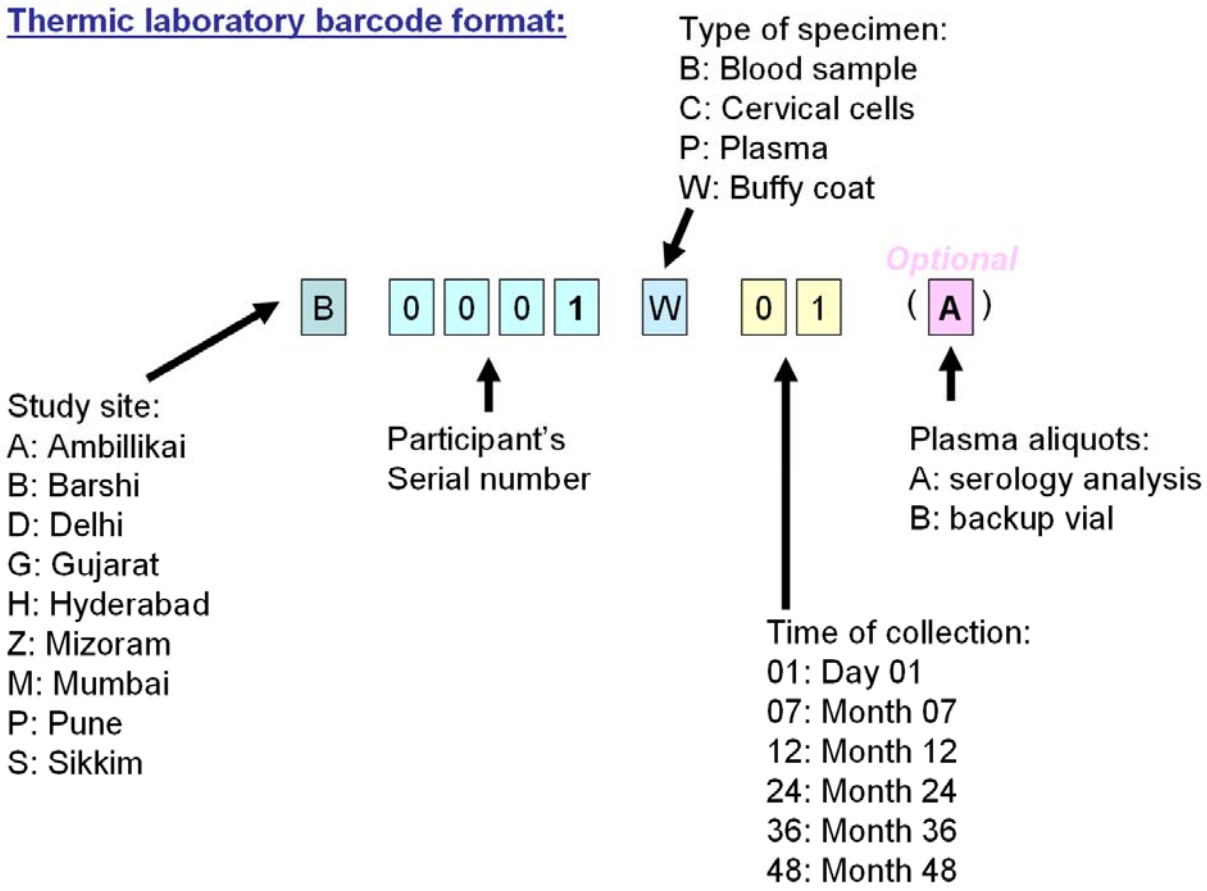
	This barcode label should be stuck on the "**participant's file**" to identify each file at the time of first registration in the field clinic.
	This barcode label should be stuck on the "**informed consent form**" to identify this form (only on the study copy, not on the one given to the participant) at the time of first registration in the field clinic. When the patient reaches 18 years, the "consent form major" barcode label should be stuck on the duly completed and signed "**major informed consent form**".
	This barcode label should be stuck on the "**participant's ID card**" to identify each participant at the time of first registration in the field clinic.

	This barcode label should be stuck on the "**household form**" to link each participant to her household. If a household contains more than one eligible participant, stick each participant's barcode in the margin to link them to this household.
	This barcode label should be stuck on the "**Vaccination form**" on day 1, to confirm her presence at the vaccination clinic at the time of registration. This barcode label should also be read by the mobile field barcode reader at each vaccination visit to link the participant to vaccination at the time of registration in the field clinic.
	This barcode label should be stuck on the "**follow-up**" form at month 7, to confirm the presence of this participant at this specific follow-up at the time of registration in the field clinic. This barcode label should also be read by the mobile field barcode reader at each follow-up visit to link the participant to vaccination at the time of registration in the field clinic.
	If applicable, this barcode label should be stuck on the "**update/discontinuation**" form to record that we have updated information on this participant at the time of registration during any visit. This barcode label should also be read by the mobile field barcode reader at each update visit to link the participant to vaccination at the time of registration in the field clinic.

SCREENING 1 GIRL FORM 	If applicable, this barcode label should be stuck on the "**screening**" form to confirm that we have done a first cervical cancer screening for this eligible participant in the field clinic. This barcode label should also be read by the mobile field barcode reader at each screening to link the participant to screening at the time of registration in the field clinic.
SCREENING 2 GIRL FORM 	If applicable, this barcode label should be stuck on the "**screening**" form to confirm that we have done a second cervical cancer screening for this eligible participant in the field clinic. This barcode label should also be read by the mobile field barcode reader at each screening declaration to link the participant to screening at the time of registration in the field clinic.
SCREENING MOTHER FORM 	If applicable, this barcode label should be stuck on the "**screening**" form to confirm that we have done a cervical cancer screening for the participant's mother in the field clinic. This barcode label should also be read by the mobile field barcode reader at each screening declaration to link the participant to screening at the time of registration in the field clinic.
PREGNANCY 1 	If applicable, this barcode label should be stuck on the "**pregnancy**" form to record a first pregnancy for this participant. This barcode label should also be read by the mobile field barcode reader to link the participant to pregnancy at the time of declaration in the field clinic.
PREGNANCY 2 	If applicable, this barcode label should be stuck on the "**pregnancy**" form to record a second pregnancy for this participant. This barcode label should also be read by the mobile field barcode reader to link the participant to pregnancy at the time of declaration in the field clinic.

ACCEPTABILITY FORM 	If applicable, this barcode label should be stuck on the "**acceptability**" form to associate the participant to the acceptability study. This barcode label should also be read by the mobile field barcode reader to link this form to the participant's digital folder.
ADVERSE EVENT 1 	This barcode label should be stuck on the "**adverse events**" or "**serious advserse events**" forms during any visit, to confirm the existence of a first AE or SAE for this participant. This barcode label should also be read by the mobile field barcode reader to link this AE/SAE form to the participant's digital folder.
ADVERSE EVENT 2 	This barcode label should be stuck on the "**adverse events**" or "**serious advserse events**" forms during any visit, to confirm the existence of a new AE or SAE for this participant. This barcode label should also be read by the mobile field barcode reader to link this AE/SAE form to the participant's digital folder.
ADVERSE EVENT 3 	This barcode label should be stuck on the "**adverse events**" or "**serious advserse events**" forms during any visit, to confirm the existence of a new AE or SAE for this participant. This barcode label should also be read by the mobile field barcode reader to link this AE/SAE form to the participant's digital folder.
ADVERSE EVENT 4 	This barcode label should be stuck on the "**adverse events**" or "**serious advserse events**" forms during any visit, to confirm the existence of a new AE or SAE for this participant. This barcode label should also be read by the mobile field barcode reader to link this AE/SAE form to the participant's digital folder.
ADVERSE EVENT 5 	This barcode label should be stuck on the "**adverse events**" or "**serious advserse events**" forms during any visit, to confirm the existence of a new AE or SAE for this participant. This barcode label should also be read by the mobile field barcode reader to link this AE/SAE form to the participant's digital folder.

C.2.f Cryo specimen barcode presentation:



For each study site we define a serial range to separate:

- 2 doses vs 3 doses participants to facilitate logistics
- Sero-testing group (15% of participants) vs non sero-testing group (85%)
- An extra 5% of security stickers for each category

Required barcode format for the non sero-testing group participants:

- 3 doses (1);
- 3 doses – security (2);
- 2 doses (3);
- 2 doses – security (4);

		3 doses				2 doses			
		3 doses (1)		Security (2)		2 doses (3)		Security (4)	
		Total	Serial	Total	Serial	Total	Serial	Total	Serial
Barshi	B	2975	1 > 2975	150	2976 > 3126	2975	5001 > 7975	150	7976 >8126
Mumbai	M	1275	1 > 1275	64	1276 > 1341	1275	5001 > 6275	64	6276 >6340
Pune	P	1275	1 > 1275	64	1276 > 1341	1275	5001 > 6275	64	6276 >6340
Ambillikai	A	1275	1 > 1275	64	1276 > 1341	1275	5001 > 6275	64	6276 >6340
Gujrarat	G	425	1 > 425	21	426 > 446	425	1001 > 1425	21	1426 > 1446
Delhi	D	425	1 > 425	21	426 > 446	425	1001 > 1425	21	1426 > 1446
Hyderabad	H	425	1 > 425	21	426 > 446	425	1001 > 1425	21	1426 > 1446
Mizoram	Z	212	1 > 212	11	213 > 224	212	501 > 712	11	713 > 724
Sikkim	S	212	1 > 212	11	213 > 224	212	501 > 712	11	713 > 724
Total **(17852)**		**8499**		**427**		**8499**		**427**	

Label sheet format for each non-sero-testing group participants:

Specimen type	Field collection	A Lab	B Lab
M07 Plasma:	B 0001 **B** 07	B 0001 **P** 07 A	B 0001 **P** 07 B
M07 Buffy coat:		B 0001 **W** 07	
EX1 Cx Cells:	B 0001 **C** 1	B 0001 **C** 1 A	B 0001 **C** 1 B
EX2 Cx Cells:	B 0001 **C** 2	B 0001 **C** 2 A	B 0001 **C** 2 B
EX3 Cx Cells:	B 0001 **C** 3	B 0001 **C** 3 A	B 0001 **C** 3 B
EX4 Cx Cells:	B 0001 **C** 4	B 0001 **C** 4 A	B 0001 **C** 4 B

28 labels per participant / 2 empty / 7 rows

Note:
These participants have only one blood sample taken at month 7.

- First column: instruction column
- Second column: used during blood or cell collection by the field medical team
- Third column: used for the first aliquot "A" preparation (or buffy coat) by the laboratory staff
- Fourth column: used for the second aliquot "B" (security) preparation (or buffy coat) by the laboratory staff

Required barcode format for the sero-testing groups participants:

- 3 doses – sero-testing group (5);
- 3 doses – sero-testing group – security (6);
- 2 doses – sero-testing group (7);
- 2 doses – sero-testing group – security (8);

		3 doses				2 doses			
		2 doses (5)		*Security (6)*		*sero-testing (7)*		*sero-testing security (8)*	
		Total	*Serial*	*Total*	*Serial*	*Total*	*Serial*	*Total*	*Serial*
Barshi	B	525	4001 > 4525	25	4526 > 4551	525	9001 > 9525	25	9526 > 9551
Mumbai	M	225	4001 > 4225	12	4226 > 4238	225	9001 > 9225	12	9226 > 9238
Pune	P	225	4001 > 4225	12	4226 > 4238	225	9001 > 9225	12	9226 > 9238
Ambillikai	A	225	4001 > 4225	12	4226 > 4238	225	9001 > 9225	12	9226 > 9238
Gujrarat	G	75	501 > 575	5	576 > 580	75	1501 > 1575	4	1576 > 1580
Delhi	D	75	501 > 575	5	576 > 580	75	1501 > 1575	4	1576 > 1580
Hyderabad	H	75	501 > 575	5	576 > 580	75	1501 > 1575	4	1576 > 1580
Mizoram	Z	38	401 > 438	5	439 > 440	38	901 > 938	2	939 > 940
Sikkim	S	38	401 > 438	2	439 > 440	38	901 > 938	2	939 > 940
Total (**3156**)		1501		77		1501		77	

Label Sheet format for each sero-testing group participants:

Specimen type	Field collection	A Lab	B Lab
D01 Plasma:	B 4001 B 01	B 4001 P 01 A	B 4001 P 01 B
M07 Plasma:	B 4001 B 07	B 4001 P 07 A	B 4001 P 07 B
M07 Buffy coat:		B 5001 W 07	
M12 Plasma:	B 4001 B 12	B 4001 P 12 A	B 4001 P 12 B
M24 Plasma:	B 4001 B 24	B 4001 P 24 A	B 4001 P 24 B
M36 Plasma:	B 4001 B 36	B 4001 P 36 A	B 4001 P 36 B
M48 Plasma:	B 4001 B 48	B 4001 P 48 A	B 4001 P 48 B
EX1 Cx Cells:	B 4001 C 1	B 0001 C 1 A	B 0001 C 1 B
EX2 Cx Cells:	B 4001 C 2	B 0001 C 2 A	B 0001 C 2 B
EX3 Cx Cells:	B 4001 C 3	B 0001 C 3 A	B 0001 C 3 B
EX4 Cx Cells:	B 4001 C 4	B 0001 C 4 A	B 0001 C 4 B

48 labels per participants / 2 empty / 12 rows

Note: *These participants have blood samples taken day 1, months 7, 12, 24, 36 and 48.*

C.2.g Barcode reader:

We will use 2 types of barcode readers:

- The mobile barcode reader for the field tracking system;
- The office barcode reader for the data entry/lab processing.

Mobile barcode reader:
It is a small barcode data collector including a flash data memory to ensure thousands of codes can be stored securely.
The USB interface acts not just to communicate with the computer to exchange data but charge the built-in-Li-Ion battery.
There is also a real time clock to facilitate date and time stamping.
It is the ideal barcode data collector solution for scanning medical research.
This barcode will be used on the field to track participant attendance to the vaccination/follow-up visits.

Office barcode reader:

This barcode reader will allow to identify the digital participant folder in the database to save time and to avoid any data entry errors.

Similarly we will also use barcodes to read the specimen barcodes to save time and avoid errors.

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

VACCINATION FORM

Id number:	B-2-001-002-0157-03 *Site Group PHC Village House Number Serial*	VACCINATION SERO B4416VD01 3
Name:		

C.3 Heading:

At the beginning, each questionnaire will contain an identification section to allow tracking a participant's localization and to allow her unique identification.

This section will contain the unique number and a barcode.

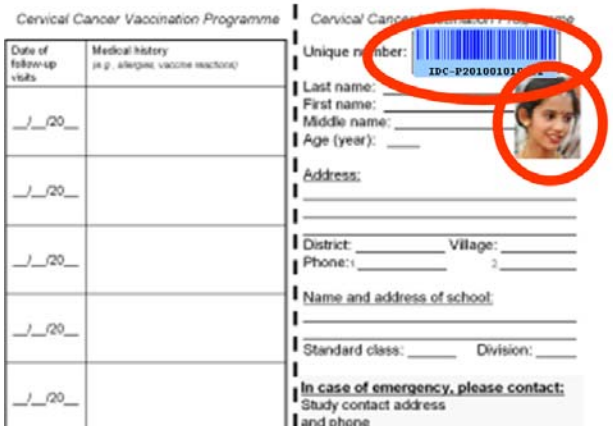
Example: The following Id-Number (B-2-001-002-0157-03) is associated to the Barcode number (B4416)

For the entire duration of the project, each specific participant will have:

- The same unique number (Id number);
- The same Barcode number (serial number).

Each document (consent, ID-card, questionnaires, check lists) and specimens (blood, urine, HPV cells) will have the same number for a specific participant.

D. Accuracy of participant identification

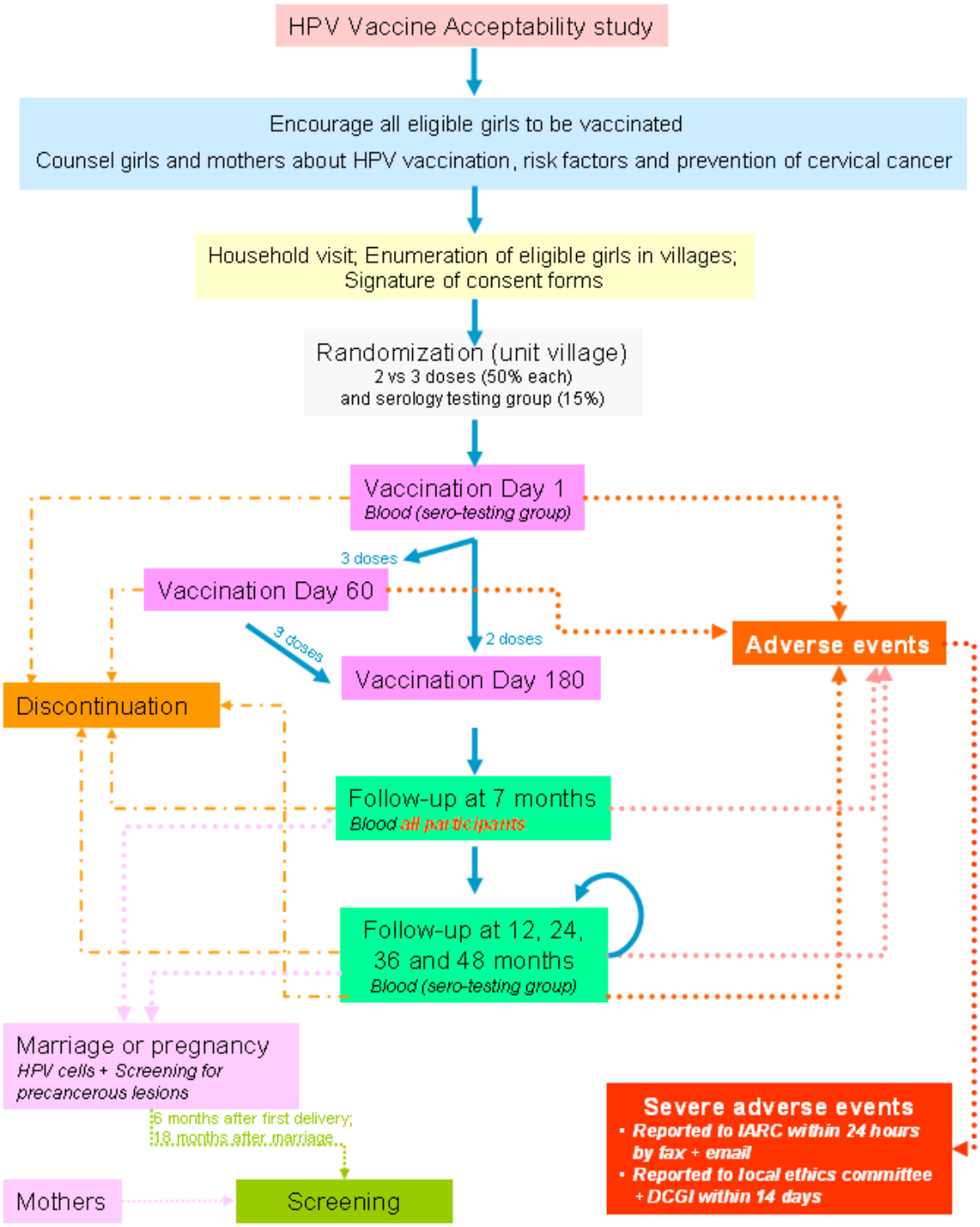


Use at least two participant identifiers when vaccinating and/or taking blood samples:

- **unique number (barcode), and**
- **photo**

Compare this information at the time of registration with the participant

E. Data flow:


HPV Vaccine Acceptability study
Encourage all eligible girls to be vaccinated
Counsel girls and mothers about HPV vaccination, risk factors and prevention of cervical cancer
Household visit; Enumeration of eligible girls in villages;
Signature of consent forms
Randomization (unit village)
2 vs 3 doses (50% each)
and serology testing group (15%)
Vaccination Day 1
Blood (sero-testing group)
3 doses
Vaccination Day 60
3 doses
2 doses
Vaccination Day 180
Adverse events
Discontinuation
Follow-up at 7 months
Blood all participants
Follow-up at 12, 24,
36 and 48 months
Blood (sero-testing group)
Marriage or pregnancy
HPV cells + Screening for
precancerous lesions
6 months after first delivery;
18 months after marriage
Mothers
Screening
Severe adverse events
• Reported to IARC within 24 hours by fax + email
• Reported to local ethics committee + DCGI within 14 days

F. When? What and why? Who? Action?

When?	What and Why?	Who?	Action?
Before D0	**HPV vaccine acceptability study** *Collect data about awareness and acceptability*	*HW*	*Acceptability form*
D0	**Enumeration (all)** *Identification of eligible girls; consent forms; collection of household and individual data + photo of participating girls (all)*	*HW*	*Consent form* *Household form* *Vaccination form* *ID-Card + Photo* *Invitation to vaccination clini*
D1	**First vaccination (both groups)** *Identification + registration / medical exam + vaccination + blood (sero group)*	*HW* *Nurse* *Doctor +*	*Vaccination form* *Blood sample taken** *Adverse event form** *Discontinuation/update**
D60	**Second vaccination (3 doses group)** *Identification + registration / medical exam + vaccination*	*HW* *Nurse* *Doctor +*	*Vaccination form* *Adverse event form** *Discontinuation/update**
D180	**Third vaccination (both groups)** *Identification + registration / medical exam + vaccination*	*HW* *Nurse* *Doctor +*	*Vaccination form* *Adverse event form** *Discontinuation/update**
M7	**Follow-up (all)** *Identification + registration / medical exam + blood sample (all)*	*HW* *Nurse* *Doctor +*	*Follow-up form* *Blood sample taken** *Adverse event form** *Discontinuation/update**
M12, M24 M36, M48	**Follow-up (all)** *Identification + registration / medical exam + blood sample (sero group only) + speculum examination (after delivery or married girls only)*	*HW* *Nurse* *Doctor +*	*Follow-up form* *Blood sample taken** *Adverse event form** *Discontinuation/update**
ANY TIME — Problem	**Adverse event (if applicable)** Report the problem collected and report severe adverse events+ to PI/IARC within 24 hours/7 days	*Nurse* *Doctor +*	*Adverse event form* *Severe adverse event form**
ANY TIME — *Adverse experience, Investigator's decision, Migration, Withdrew consent, Pregnancy, Lost of follow-up, Clinical trial terminated;*	**Discontinuation or Update** Report the reason and information about the discontinuation / or last participant update data	*HW* *Nurse* *Doctor+*	*Discontinuation/update*
ANY TIME — Marriage or After delivery	**Screening (if applicable)** *Girl identification and registration* *Medical and vaccination data collection* *Sample identification (all)*	*Nurse* *Doctor +*	*Screening form*
ANY TIME — After delivery	**Pregnancy (if applicable)** *Report the data about the pregnancy collected*	*HW* *Nurse* *Doctor +*	*Pregnancy form*

* *If applicable* + *In presence of doctor*

G. Checklist

Enumeration (D0)	
Procedures	___ Number each house in the village in a proper sequence with paint and brush ___ Enumerate each household member using **Household form/Enumeration form** ___ Identify eligible girls in the household
Forms	• Form: Household

Day before vaccine clinic (between D0 and D1)	
Procedures	___ Administer informed consent to the parent(s)/legal guardian and get the ICF signed by the parent(s)/legal guardian and participant girl ___ Take photo of the eligible girl(s) in the household with a digital camera ___ Collect information (socio-demographic and reproductive) about the eligible girl on the **Vaccination form** (D1) ___ Give personal invitation card to the eligible girl indicating the date, time and venue of the vaccination clinic in the village

Forms	• Form: Informed Consent
	• Form: Vaccination form
	  ○ section A: eligibility
	  ○ section B: participant's information

First day of vaccination (Day 1)	
Procedures	___ Retrieve the participant's file when the girl comes to the registration desk and shows her invitation card ___ Give the participant ID card to her and screening invitation to her mother ___ Take out one barcode label from her file and stick it on the vaccine check list ___ Prepare the blood collection tube with the barcode label if applicable (sero- testing group), stick one to the sample check list and one to the blood collection form. ___ Before vaccination, update participant's personal status (marital, contact details, school, etc.), participant history, collect vital signs on the forms mentioned in the **update section** ___ Take out the vaccine from the ice box, remove the vaccine label, stick on the vaccination record form and update the form mentioned in the **update section** ___ Make the girl comfortable and inject the first dose of the Vaccine ___ Instruct her to wait for 30 minutes at the clinic and observe her for any side effects ___ If there is any adverse event, update the **adverse event form** and manage as per the AE management guidelines ___ After half an hour, instruct the girl to report for any adverse event after she goes home using the contact numbers given on her ID card ___ Write the date, time and venue of vaccination clinic for the next dose on the Participant's ID card

Forms	• Form: Vaccination
	  ○ section B: Participant's information (D1)
	  ○ section C: Participant's history (D1/M2/M6)
	  ○ section D: Vital signs (D1/M2/M6) (See update section)
	  ○ section E: Urine pregnancy test (M2/M6)
	  ○ section F: Blood collection (only for sero-testing group) (D1)
	  ○ section G: Vaccination record (D1/M2/M6) (See update section)
	• Form: Adverse event form (if applicable)
	• Form: Serious adverse event form (if applicable)
	• Form: Discontinuation/update (if applicable)

Vaccination (Day 60 and/or Day 180)	
Procedures	___ Retrieve participant's file when she comes to the registration desk with her ID card ___ If the girl got married, ask her to sign a new consent form with her ID card ___ Take out one barcode label from her file and stick it on the vaccine check list ___ Before vaccination, update participant's personal status (marital, contact details, school, etc.), participant history, collect vital signs on the form ___ Take out the vaccine from the ice box, remove the vaccine label, stick on the vaccination record form ___ Make the girl comfortable and inject the 2nd/ 3rd dose of the Vaccine ___ Instruct her to wait for 30 minutes at the clinic and observe her for any side effects ___ If there is any adverse event, update the **adverse event form** and manage as per the AE management guidelines ___ After half an hour, instruct the girl to report for any adverse event after she goes home using the contact numbers given on her ID card ___ Write the date, time and venue of vaccination clinic for the next dose/month 7 follow up on the Participant's ID card

Forms	• Form: Vaccination
	  o section C: Participant's history (D1/M2/M6)
	  o section D: Vital signs (D1/M2/M6) (See update section)
	  o section E: Urine pregnancy test (M2/M6)
	  o section G: Vaccination record (D1/M2/M6) (See update section)
	• Form : Adverse events (if applicable)
	• Form: Serious adverse event form (if applicable)
	• Form: Informed consent form for major
	• Form: Discontinuation/update (if applicable)

Follow-up (Month 7)	
Procedures	___ Retrieve the participant's file when she comes to the registration desk with her ID card ___ If the girl got married, ask her to sign a new consent form ___ Take out one barcode label from her file and stick on the follow up check list ___ Prepare the blood collection tube with the barcode label, stick one to the sample check list and one on the blood collection form ___ Update participant's personal status (marital, contact details, school, etc.), participant history on the forms mentioned below ___ Write the date, time and venue of next follow up visit on Participant's ID card ___ Also update the forms mentioned in the next section

Forms	• Form: Follow-up
	  ○ section A: Participant's information and history
	  ○ section B: Blood collection
	  ○ section C: Speculum examination (if applicable)
	• Form : Adverse events (if applicable)
	• Form: Serious adverse event form (if applicable)
	• Form: Informed consent form for major
	• Form: Discontinuation/update (if applicable)

Follow-up (M12/M24/M36/M48)	
Procedures	___ Maintain record of marriage, pregnancy and due date of delivery of all the Participants ___ Retrieve the participant's file when the girl comes to the registration desk with her ID card ___ If the girl got married, ask her to sign a new consent form ___ Take out one barcode label from her file and stick on the follow up check list ___ During yearly follow up visits, prepare the blood collection tube with the barcode label if applicable (sero-testing group), stick one to the sample check list and one to the blood collection form ___ Prepare barcode labels for collection of cervical cells and screening forms for the participants who have delivered 6 months back
Forms	• Form: Follow-up (update at M12/M24/M36/M48 o section A: Participant's information and history o section B: Blood collection o section C: Speculum examination (if applicable) • Form : Adverse events (if applicable) • Form: Serious adverse event form (if applicable) • Form: Informed consent form for major • Form: Discontinuation/update (if applicable) • Form: Pregnancy (if applicable) • Form: Screening (if applicable)

Any visit (Any)- Update the following forms at any visit if required	
Forms	• Form : Adverse events (if applicable) • Form: Serious adverse event form (if applicable) • Form: Informed consent form for major • Form: Discontinuation/update (if applicable) • Form: Pregnancy (if applicable) • Form: Screening (if applicable)

H. Participant clinical research file

● Each participant to have a separate file containing all the clinical research forms.

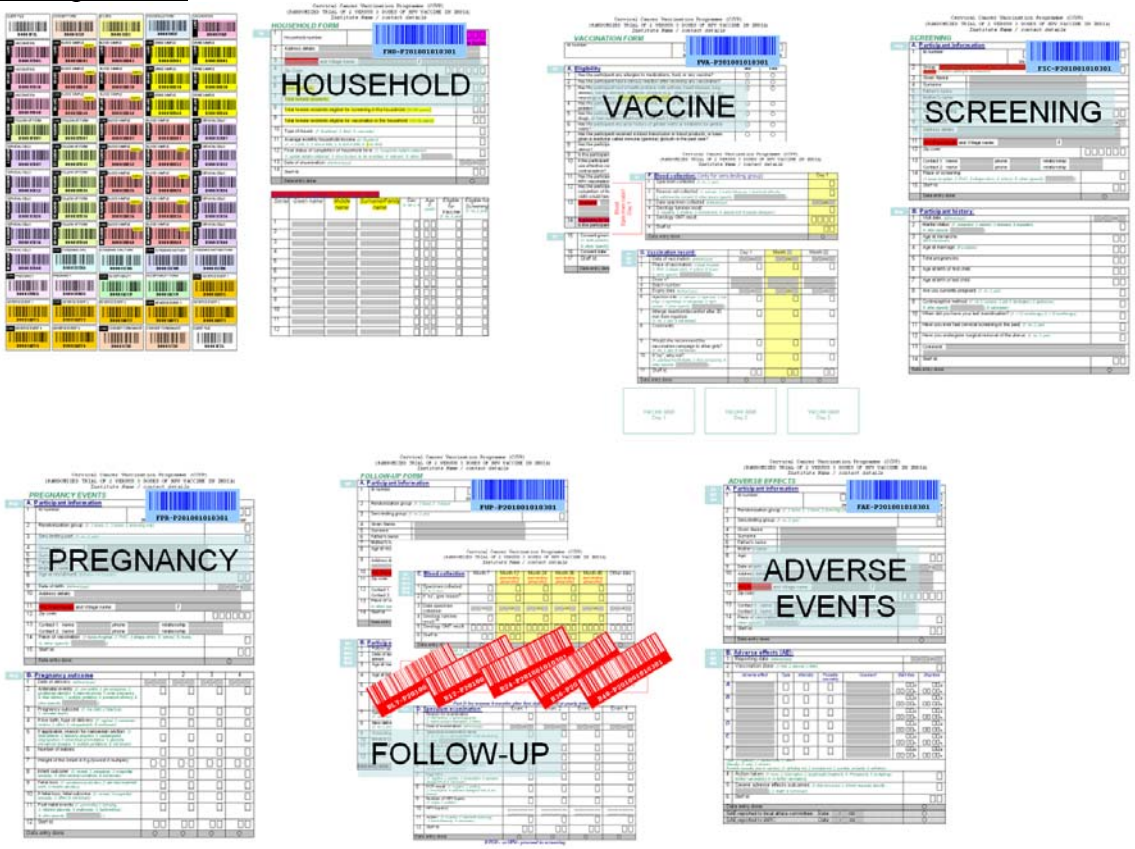
● The barcode printed labels will be added and stored in the participant's file.

● A set of all clinical research forms for each participant to be vaccinated on a particular day should be prepared in advance at the site HQ.

● All clinical research files of participants expected for vaccination to be stored in a separate binder and taken to the field for vaccination day.

● A number of empty clinical research forms should be also available on the day of the clinics to record unforeseen data (adverse events, screening, pregnancy).

Participant file:



I. Solutions to avoid writing confusion

Characters confused	Solution
1 and 7	This confusion arises if ones are written with an initial upward stroke (for example ). If this is the situation, then always write sevens with a horizonthal line through them (as the French do), that is  . A simpler solution may be to insist that ones are written with a single stroke (for example).
O (letter O) and 0 (number zero)	Note (1). Write the number 0 (zeros) with a line through them, that is  .
4 and 9	Write the number 4 like this  .
4 and 7	These digits may be confused if sevens are written with a horizontal line through them ! Instruct field-workers to make sure that the top of the seven is written horizontally.
6 and 9 (upside-down)	Relevant when coding laboratory specimens (for example, is it 61 or 19 ?). Draw a horizontal line under all numbers. For example 19 or 61
2 and Z	Note (1). Always write Z with a horizontal line through it, that is  .
5 and S	Note (1). Always write 5 using 2 pen strokes.
O (letter O) and Q	Note (1) Always write Q using 2 pen strokes.
I and 1	Note (1). Always write I (letter i) with 'hat and shoes', not as a single stroke, that is I not .
U and V	Avoid both letters as codes as far as possible (will be needed for names).

Note (1). Avoid using the alphabetical character in data fields that may contain both alphabetical and/or numerical information.

J. Standards for taking identity photo

Standards for taking identity photographs

Format:
The face is entirely shot from the bottom of the chin to the top of the head. The photo must show full front view of the bearer.

Photo quality:
The photo must be clean, without folds or stains.

Laser printer:
Make sure the print quality, paper and the resolution is acceptable.

Brightness / contrast / colors:
The photo should be free from over- or under-exposure. Take care not to have any shadow on the face or background.

Hair and eyes:
The eyes must be open, the subject's face clearly seen, i.e, no hair should obscure the eyes.

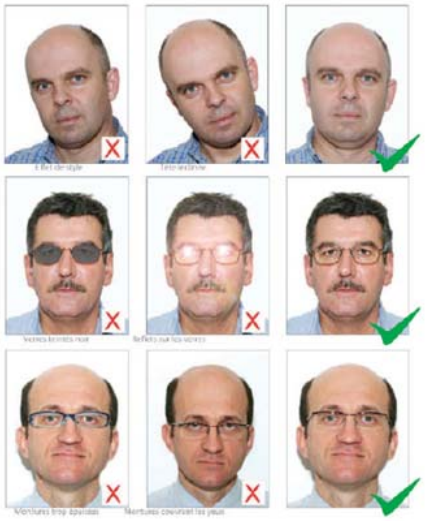
Position:
The subject must face the camera with her head straight.

Background / framing:
The background must be plain and light in colour, head straight, i.e. the imaginary line joining the center of the eyes should be parallel to the background.

Red Eye:
To avoid red eyes, use the digital camera with "red eye" option.

Sunglasses: The eyes must be clearly visible without light reflection on glasses, which must not be fitted with colored lenses

Glasses frames: avoid thick frames. Frames must not hide the eyes



The head coverings: The head should not be covered.

Expressions: The photo must represent the subject alone with a straight face and mouth closed.

All the partipant pictures for a specific village will be printed to generate the "photo ID sheet" in black and white with a proper resolution using the "Photo printing Wizard / contact sheet 35 per pages" option in Windows.

For each village the team will generate 3 copies of the photo ID sheet:

- *One to help mobilizator to locate eligible participant in villages (normal paper);*
- *One to stick each ID photo on the participant Id-card (label paper);*
- *One to stick each ID photo on the participant file (lable paper).*

More detail about photo management will be available in the Operations Manual – Information System.

When a participant gets married we will take a new picture during the follow-up process.

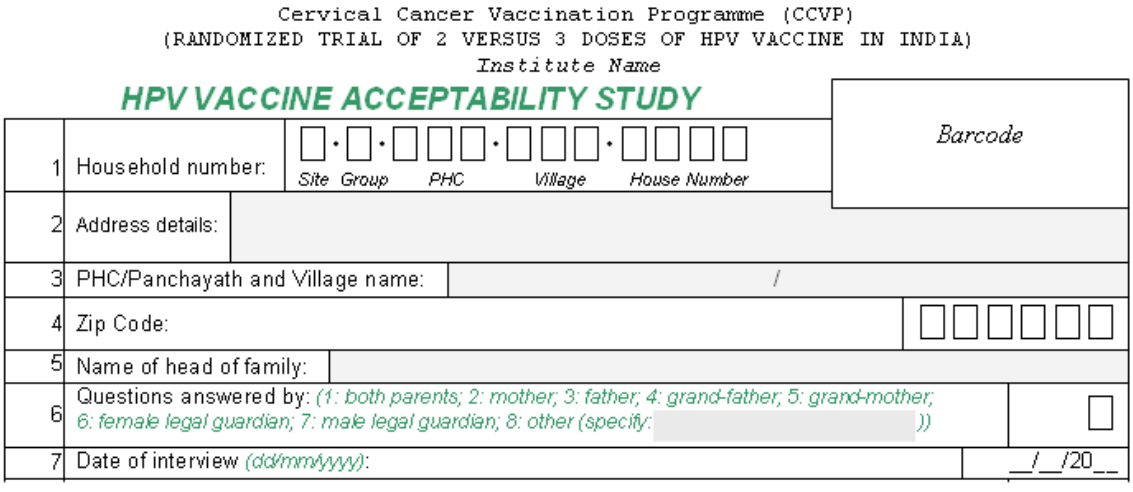
2. Questionnaires

A. HPV vaccine acceptability study form

This form is used to collect acceptability information from future study participants. This is an interviewer-administered form and is administered before inclusion of the participants.

HPV vaccine acceptability study

A	Field on the form	Instructions
1	Household number	Indicate the household number according to the defined format (11 characters): - Site: one letter to codify the study site - Group: one digit to codify the randomization group (2 or 3 doses) according to the localization - PHC: three digits to codify the Primary Health Centre (PHC) - Village: three digits to codify the village House number: four digits to codify the house number in the village
2	Address details	Indicate the address (with full details) to facilitate participant follow-up.
3	PHC/Panchayath and Village name	Indicate the PHC/Panchayath and village name to facilitate the participant follow-up (e.g. include details such as behind the bus station).
4	Zip Code	Indicate the zip code to facilitate participant follow-up.
5	Name of head of family	Indicate the name of the head of family to facilitate house localization.
6	Questions answered by	Indicate the person who answered the question according to the list.
7	Date of interview	Record the actual date of the interview visit (dd/mm/yyyy).



Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

HPV VACCINE ACCEPTABILITY STUDY

1	Household number: □·□·□□□·□□□·□□□□ (Site Group PHC Village House Number)	Barcode
2	Address details:	
3	PHC/Panchayath and Village name: /	
4	Zip Code:	□□□□□□
5	Name of head of family:	
6	Questions answered by: (1: both parents; 2: mother; 3: father; 4: grand-father; 5: grand-mother; 6: female legal guardian; 7: male legal guardian; 8: other (specify:))	□
7	Date of interview (dd/mm/yyyy):	__/__/20__

8	Total number residents in house	Indicate the total permanent residents in the house (exclude temporary visitors or neighbors in the count).
9	Total adolescent girls	Indicate the total permanent adolescent girls resident in the house (exclude temporary visitors or neighbors in the count). Adolescent age limit is between 15 to 19. (IARC)
10	Type of house	Indicate the type of house according to the list (thatched, tiles, concrete).
11	Monthly income	Indicate the average monthly household income (in rupees).
12	Parent education	Indicate the highest level of either parent's education according to the list.
13	Respondent's occupation	Indicate respondent's occupation according to the list.
14	Respondent attended the village cervical cancer prevention programme	Indicate whether the respondent attended the village cervical cancer prevention programme or not.
15	Heard about any cancer	Indicate whether the respondent heard about any cancer. If "no" do not ask questions 20 to 26, go to question 27.
16	Name a few cancers	If applicable, indicate the names of a few cancers that the participant knows.
17	Heard about cervical cancer	If applicable, indicate whether the participant heard about cervical cancer or not.
18	How did you hear about cervical cancer	If applicable, indicate how the participant heard about cervical cancer.
19	Have you	If applicable, indicate only one reply for the following affirmation: "Have you" according to the list. If "not know", go to question 24.
19a	Treated	If applicable and if so, indicate how she was treated according to the list.
19b	Patient outcome	If applicable and if so, indicate what the patient's outcome was according to the list.
20	Heard about HPV	If applicable, indicate whether the participant already heard about Human Papilloma Virus (HPV) infection which causes cervical cancer.
21	Use tobacco	If applicable, indicate if the participant uses tobacco in any form (smoking or chewing).

8	Total number residents in the house:	☐☐
9	Total number of adolescent girls in the house *(between 10-18 (<19) years)*:	☐☐
10	Type of house: *(1: thatched; 2: tiled; 3: concrete)*	☐☐
11	Average monthly household income *(in Rupees)*: *(1: < 2 000; 2: 2 000-4 999; 3: 5 000-9 999; 4: ≥10 000)*	☐
12	Highest level of education of the respondent: *(1: uneducated; 2: primary (1 to 4 grades of schooling); 3: secondary (5 to 10 grades of schooling); 4: some college; 5: completed with a graduate degree and above)*	☐
13	Respondent's occupation: *(1: housewife/unemployed; 2: farmer;3: government service; 4: private service; 5: self-employed)*	☐
14	Has the respondent attended the village cervical cancer prevention programme? *(1: no; 2: yes; 3: has not yet been arranged)*	☐
15	Have you ever heard about any cancer? *(1: no; 2: yes)* ***If 'no' go to question 24***	☐
16	If yes, name a few cancers that you know: / /	
17	Have you heard about cervical cancer? *(1: no; 2: yes)*	☐
18	How did you hear about cervical cancer? *(1: doctor/nurses; 2: health workers; 3: radio or TV; 4: know someone who has suffered; 5: group meeting in the village; 8: other (specify:)*	☐
19	Have you: *(1: known a relative who suffered of cervical cancer; 2: known a woman from your village who suffered of cervical cancer; 3: known someone in a nearby village who suffered of cervical cancer; 9. None of the above)*	☐
19a	If so, how was she treated? *(1: surgery; 2: chemotherapy; 3: radiotherapy; 4: don't know)*	☐
19b	If so, what was that patient's outcome? *(1: died; 2: recovered/surviving)*	☐
20	Have you heard of Human Papilloma Virus (HPV) infection which causes cervical cancer? *(1: no; 2: yes)*	☐
21	Do you use tobacco in any form (smoking/chewing)? *(1: no; 2: yes)*	☐

22	Risk factors cervical cancer	If applicable, indicate whether the participant knows the risk factors for developing cervical cancer. Complete Q26a to Q26h even if the answer to Q26 is "don't know". Ask the participant if they can guess about any of the risk factors listed in the Q26a-26h.
22a	Early age at marriage	Indicate whether the participant got married young.
22b	Early age at delivery	Indicate whether the participant was young when her 1st child was born.
22c	Poor spacing between 2 child births	Indicate whether the participant had 2 children in less than 2 years. (UNICEF recommendation)
22d	Multiparity	Indicate whether the participant had more than 1 child.
22e	Multiple sexual partners	Indicate whether the participant had multiple sexual partners.
22f	Non-use of condoms	Indicate whether the participant does not use condoms.
22g	Poor genital hygiene	Indicate whether the participant has poor personal hygiene.
22h	Use of tobacco	Indicate whether the participant uses tobacco.
23	Heard about the screening tests cxca	Indicate whether the participant heard about the screening tests to detect early cancerous changes on the cervix.
24	Undergone a screening test cxca	If appropriate for women between 30-59 years, indicate if the participant has ever undergone a screening test for early detection of cervical cancer. If the participant is not eligible or if the reply is "no", leave this field and next two fields empty and go to question 29.
25a	If yes, report	If appropriate and if previous reply was "yes", indicate the report findings. If the participant is not eligible, leave this field empty.
25b	If abnormal, treatment	If appropriate and if previous reply was "abnormal", specify the abnormalities. If the participant is not eligible, leave this field empty.
26	Daughter illness	Indicate whether the participant's daughters suffered from any major illness in the recent past.
27	If yes, specify	If previous reply was "yes", specify the illness in detail. If the reply to the previous question was "no", leave this field empty.

22	Do you think the following factors increase the chance of getting cervical cancer?	
22a	Early age at marriage/onset of sexual activity *(<18 yrs)*: *(1: no; 2: yes; 3: don't know)*	☐
22b	Early age at delivery *(<20 yrs)*: *(1: no; 2: yes; 3: don't know)*	☐
22c	Poor spacing between 2 child births: *(1: no; 2: yes; 3: don't know)*	☐
22d	Multiparity: *(1: no; 2: yes; 3: don't know)*	☐
22e	Multiple sexual partners: *(1: no; 2: yes; 3: don't know)*	☐
22f	Non-use of condoms: *(1: no; 2: yes; 3: don't know)*	☐
22g	Poor genital hygiene: *(1: no; 2: yes; 3: don't know)*	☐
22h	Use of tobacco: *(1: no; 2: yes; 3: don't know)*	☐
23	Have you heard about the screening tests to detect early cancerous changes on the cervix? *(1: no; 2: yes)*	☐
24	***Only for women between 30-59 yrs. If 'no' go to question 29*** Have you ever undergone a screening test for early detection of cervical cancer? *(1: no; 2: yes)*	☐
25a	If 'yes', what was the report? *(1: normal; 2: abnormal)*	☐
25b	If abnormal, what treatment were you given?	
26	Has your daughter(s) suffered from any major illness in the recent past? *(1: no; 2: yes)*	☐
27	If 'yes', specify the illness:	

28	Whom do they consult for illness	Indicate who the participant generally consults for her illness.
29	Who takes the decision for children health	Indicate who takes decisions for the participant's children's health and well-being. Specify other choices(s) if needed.
30	Heard about vaccine	Indicate whether the participant heard about vaccines.
31	Can you tell the names of some commonly used vaccines	Do not read the names of the vaccines. Mark "yes" or "no" for the spontaneous responses for the vaccines named below. If the response to this question is "no", skip to question 35.
31a	Polio:	Mark "1", if they do not tell the name of polio vaccine. Mark "2", if they tell you about the polio vaccine. If previous Q33 reply is "no", leave this field empty.
31b	Measles:	Mark "1", if they do not tell the name of measles vaccine. Mark "2", if they tell you about the measles vaccine. If previous Q33 reply is "no", leave this field empty.
31c	BCG:	Mark "1", if they do not tell the name of BCG vaccine. Mark "2", if they tell you about the BCG vaccine. If previous Q33 reply is "no", leave this field empty.
31d	DPT:	Mark "1", if they do not tell the name of DPT vaccine. Mark "2", if they tell you about the DPT vaccine. If previous Q33 reply is "no", leave this field empty.
31e	Tetanus:	Mark "1", if they do not tell the name of Tetanus vaccine. Mark "2", if they tell you about the Tetanus vaccine. If previous Q33 reply is "no", leave this field empty.
31f	Hepatitis B:	Mark "1", if they do not tell the name of Hepatitis B vaccine. Mark "2", if they tell you about the Hepatitis B vaccine. If previous Q33 reply is "no", leave this field empty.
31g	Other	If yes, specify other vaccines the participant may have heard of.
32	Cure/prevent	Indicate whether the participant thinks that vaccines cure or prevent diseases.
33	Routine vaccination	Indicate whether the participant has routine vaccination given to for their children.
34	Explain why	If no, indicate the reason why the participant did not give routine vaccination. If yes, leave this field empty.
35	Experience with routine vaccination	Indicate the participant's experience with routine vaccination programs and services.
36	Bad experience	If bad experience, ask him/her to explain the experience. If no, leave this field empty.

28	Whom do you generally consult for her illness? *(1: PHC; 2: Private Doctor in your village; 3: Private Doctor in another village; 4: Nearby hospital)*	☐
29	Who takes the decisions for your children's health and well-being? *(1:father; 2: mother; 3: both; 4: grandparent(s); 8: other, specify:*)	☐
30	Have you heard about vaccines? *(1: no; 2: yes)*	☐
31	If yes, can you tell the names of some commonly used vaccines: *(1: no; 2: yes)* *(Do not read the names of the vaccines. Mark yes or not for the spontaneous responses for the vaccines named below)*	
31a	Polio:	☐
31b	Measles:	☐
31c	BCG:	☐
31d	DPT/Tuberculosis:	☐
31e	Tetanus:	☐
31f	Hepatitis B:	☐
31g	Other, specify:	
32	Do vaccines cure or prevent diseases? *(1: cure; 2: prevent; 9: not known)*	☐
33	Did you give routine vaccination to your children? *(1: no; 2: yes; 9: not known)*	☐
34	If 'no', explain why:	
35	How was your experience with routine vaccination program and services? *(1: good; 2: bad)*	☐
36	If 'bad', please explain the reasons:	

37	Willingness to vaccinate daughter	Indicate whether the participant is willing to vaccinate her/his daughter(s) aged between 10-18 years if such a vaccine is given as part of a study in her village.
38	If no, explain	If no, indicate the reason why the participant does not want her daughter to participate in this program. If yes, leave this field empty.
39	Final status	Indicate the final status of completion of acceptability form according to the list.
40	Interviewer name	Indicate the name of the interviewer.
41	Respondent name	Indicate the name of the respondent.
42	CRF checked by	Indicate the name of the CRF checker.

Cervical Cancer Vaccination Programme (CCVP)
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Institute Name

37	**Cervical cancer can now be prevented by vaccination** Are you willing to vaccinate your daughter(s) aged between 10-18 years if such a vaccine is given as a part of a study in your village? *(1: no; 2: yes; 3: don't have an eligible daughter)*	☐
38	If the response is 'no', please explain the reason:	
39	Final status of completion of acceptability form: *(1: complete details obtained; 2: partial details obtained;3: door locked, to be revisited; 4: refused)*	☐
40	Interviewer's name:	
41	Respondent's name:	
42	CRF checked by:	
Date of data entry: *(dd/mm/yyyy)*		__/__/20__
Data entry done:		○

B. Consent form

The main purpose of this 4-page questionnaire is to collect information on the willingness of the girls and their parents to participate in this trial. The informed consent, in the local vernacular, will be signed by each willing parent/legal guardian of the eligible girls and the participating girl during the house visit. The girls will then be interviewed for demographic and clinical history using a questionnaire and will be invited to attend the vaccination clinic in their village.

The informed consent clearly describes the study, the potential advantages and any known adverse effects of the vaccine, the importance of reporting any adverse events promptly, the requirement to avoid pregnancy during the 2 or 3-dose vaccine course (i.e. 6 months), the need for blood and cervical cell collection during follow-up and the importance of adhering to the follow-up schedules. It also describes participant's liberty to withdraw from the study at any time which will have no consequences of any sort for their routine health care opportunities.

- This document contains the full contact details of the principal investigator in the section contact details (page 3). So, each site will specify its own contact details. Provision is made to allow to add co-investivator's contact details if necessary.
- This document also contains the contact details of the IARC review board.

Following data are available on page 4:

A	Field on the form	Instructions
1	Sponsor	By default the sponsor name will be: "IARC".
2	Principal investigator	Indicate by default the name of the local principal investigator.
3	Subject initials	Indicate the patient's initials to maintain the confidentiality.
4	Subject number	Indicate the subject number in the study. Use the 5 unique numbers used on the barcode to identify the patient anonymously (one letter + serial number 4 digits).
5	Mother/father /legal guardian signature/thumb	Ask to the respondent to sign or to put his/her thumb print.
6	Mother/father/legal guardian?	Delete as appropriate.
7	Mother/father/legal guardian full name	Ask the respondent to write his/her full name.
8	Mother/father/legal guardian signature date	Indicate the date of signature by the respondent and participant girl (dd/mm/yyyy).
9	Person conducting the informed consent	Indicate the full name of the person conducting the informed consent.
10	Informed consent date	Indicate the date of the signature.
11	Hospital name and address	Indicate the name and address of the base hospital.
12	Impartial witness signature/thumb	If applicable, ask the impartial witness to put his/her signature or thumb.
13	Impartial witness signature date	If applicable, ask the impartial witness to write the date of the signature.
14	Impartial witness full name	If applicable, ask the impartial witness to put his/her full name

<Local Institution / hospital header where the clinical study is carried out>

Sponsor: IARC-WHO Principal Investigator: Dr .....

Information Sheet

Study title: Randomized trial of 2 versus 3 doses of HPV vaccine in India

Introduction

Cervical cancer is a major cause of cancer deaths in India. A majority of women with this cancer are diagnosed in late stages and it is difficult to cure cancer when the disease is very advanced. Cervical cancer is caused by infection with a very common virus called human papillomavirus (HPV). HPV infection usually occurs after the onset of sexual activity. More than 80% of married women may get this infection in their life time. Even though over 100 different types of these viruses have been identified, only 15 types cause cervical cancer. Of these cervical cancer causing types, HPV types 16 and 18 cause more than 70% of cancers. It takes several years to develop this disease after HPV infection. Screening will help to detect early cancerous changes following persistent and prolonged HPV infection well in advance, before symptoms appear. Treatment at this precancerous stage results in complete cure and prevents life threatening cervical cancer.

Vaccines have now been developed to prevent HPV 16 and 18 infections. One of these vaccines, called GARDASIL®, has been widely tested in several research settings and found to be successful in preventing HPV 16 and 18 infections and early cancerous changes due to these virus types. This vaccine also prevents HPV 6 and 11 infections which cause warts. This vaccine is now licensed in more than 80 countries and more than 12 million vaccine doses have been used so far. GARDASIL® is currently given in three intramuscular injections on days 1, 60 and 180. As per current knowledge, the protective effect of the vaccine against HPV infection and cervical precancerous lesions lasts for 5 years and we are now awaiting information on benefits beyond this period.

Like other vaccines, GARDASIL® also has some side effects, but most of these are minor. The common side effects reported are pain, redness and swelling at the injection site. Dizziness, general fatigue, fever and headache nausea and vomiting are also seen in some people. Joint pain, urticaria, rashes and seizures may occur rarely. Serious reactions like anaphylactic shock and severe shortness of breath are extremely rare.

Purpose of this study

The present study aims to test whether two doses of the HPV vaccine on day 1 and day 180 are as good and safe as 3 doses of vaccination at days 1, 60 and 180 in protecting unmarried girls between 10-18 years of age at entry into the study against HPV 16 and 18 infections and cervical cancer. Consequently, if 2 doses are found to be as good as 3 doses, this will make vaccination more simple and affordable than the current 3 doses and therefore considerably reduce the overall cost of vaccination. The villages participating in this study will be randomly allotted by computer to 2 or 3 doses of vaccine.

The Drugs Controller General of India (DCGI) and the Government authorities have approved the conduct of this study in India. This study is planned in 8 centers in India in collaboration with the World Health Organization's International Agency for Research on Cancer.

Study Procedure

The participation in this study is voluntary which means that you can decide whether or not your daughter wants to be in the study. If you don't want your daughter to be in the study, this will not prevent you or your family from availing routine health care from public health services in any way. Before your daughter can participate in the study, you will be requested to sign the informed consent form (ICF). If your daughter is 18 years old, or when she attains 18 years, we will get another signed consent form from her. Once you sign the ICF, a female health worker will interview your daughter and collect information on socioeconomic, reproductive aspects, past or present illnesses and allergies. A photograph of your daughter will be taken for identification purposes. If your daughter is eligible, she will receive the vaccination according to the allocation of your village, either 2 or 3 doses. After the vaccination your daughter will be observed for 30 min for any side-effects. If she does have any side-effects at the time of vaccination, or after going back home, she should go and report to a medical officer or a hospital, or to us. You will be given a phone number to contact us on your Identification card. Your daughter will be given a personal health card with her personal details, photo identity, and the contact details of the medical officer. She will also be given a chart indicating the date of next vaccination. If your daughter has any mild or moderate side-effects, please note these on her chart and always bring it with the Identity card during all your visits. Your daughter will be requested to come for follow-up at 7, 12, 24, 36 and 48 months after the first day of vaccination. Blood will be collected at the time of first vaccination in selected cases and at 7 months from all girls participating in this study, and subsequently in selected cases at 12, 24, 36 and 48 months after the first vaccination. The purpose of taking these blood samples is to document and compare the level of immune protection offered by the 2 or 3 doses of vaccine.

You/your daughter are requested to inform us of any change in your personal information such as change of address when your daughter gets married, when she gets pregnant and when she delivers. If she gets married during the period of vaccination, she is advised to take birth control measures until the vaccination schedule is over. The medical officer in the project will give you the necessary advice. A vaginal examination will be done 18 months after marriage, or 6 months after delivery of your first child, when cervical cells will be collected using a brush to test if there is HPV infection. This procedure is simple, painless and safe. Thereafter, a vaginal examination and cervical cell collection will be done every 12 months up to 5 years from the beginning of the study. Your daughter can withdraw from the study at any time and this will not affect either you or your daughter receiving any medical care or benefits from public health services. At any time, the medical officer in charge of the study can also decide to discontinue your daughter from this study if it is in her best interest.

All medical procedures and medications, including vaccination and interventions related to the evaluation of the effectiveness and safety of the vaccination, will be provided free of cost by the project.

Confidentiality of your daughter's personal and medical records in the study will be maintained to the full extent permitted by law. Authorized researchers from IARC, participating institutions from India and authorized personnel of Indian and other National regulatory bodies will have access to your daughter's relevant medical records for

verification of clinical study procedures and overall evaluation of the study without any of her identifying information. No information will be disclosed to anyone unrelated to the conduct and evaluation of the study. The computerized data will be password protected and will be accessible to the above researchers and authorities without personal identification details.

This study will be formally monitored by an independent Data Safety Monitoring Board (DSMB). In addition the study will be regularly reviewed by the institutional review boards in India and the Scientific Council of IARC at stipulated intervals. The results of the study will be presented at national and international conferences and in national and international medical journals and will be used to help organize effective HPV vaccination programs in India and other developing countries.

Contact details

If you have any questions about this study or if your daughter experiences any side-effects, illness or injury that you believe results from this study you may contact:

Principal Investigator Co-investigator

Name
Address
Contact No

Who has reviewed the study

This study was approved by the Human Ethic Committee and the Institutional Review Board of IARC and .....
Address
Contact No

Each participant will receive a copy of this Information Sheet.

<Enter Institution / hospital header where the clinical study is carried out>

Sponsor: IARC Principal Investigator: Dr. .....
Subject Initials: Subject Number:

Informed Consent Form (for minors)

Clinical Study Protocol Title: Randomized trial of 2 versus 3 doses of HPV vaccine in India

I, the undersigned, father/mother of ..... voluntarily agree to my daughter taking part in this study.

I have been given a detailed explanation of the nature and purpose of the study and what I will be expected to do. I understand that the vaccine may cause some side-effects and risks, and that my daughter is free to withdraw from the study at any time without the need to justify the decision. This will not affect me, my daughter or my family members availing health care from public health services in any way.

I understand that my daughter's medical records will be seen by representatives of the sponsor or their agents, auditors and regulatory authorities and I agree to disclosure of this report and any results to regulatory authorities. All data will be treated as confidential and kept for as long as required by law.

I consent to the transfer/use of my daughters coded data to/by Authorized Regulatory Bodies even if my daughter withdraws from the study.

I agree to permit archival of samples (blood and tissue) for future research purposes.

I hereby give my voluntary, free and informed consent on behalf of my daughter to take part in the study and comply with all the regulations, procedures and interventions stipulated in the study protocol.

..... Signature/thumb impression of **Father/mother/legal guardian** *(delete as appropriate)* ..... Please print name	..... Date (To be inserted personally by subject)
..... Signature/thumb impression of **Participant** ..... Please print name	..... Date (To be inserted personally by subject)
..... Signature of **Person Conducting Informed Consent** ..... Please print name < HOSPITAL NAME AND ADDRESS>	..... Date
..... Signature of **Impartial Witness** ..... Please print name	..... Date

- A copy of the informed consent form, including the information sheet and the study contact details will be given to each parents/legal guardian at the time of first vaccination on day 1. Ask them to preciously keep this document.

- Another copy of the consent form will be kept in a secure place for auditing purposes in each study site and stored in a proper way.

- When the participant will become major (18 years), a new consent will be signed by the participant herself, to replace the previous one.

- When a participant attains the age of 18 and becomes a major, she will sign a new consent form (major version) but the previous consent form signed by parents or legal guardians, will not be destroyed. It is advisable to store the consents signed by the parents/legal guardians and those signed by the participants when they become a major, in separate files.

If parents or legal guardians of any participant refuse to sign the consent form or if they do not agree with the full study process, do not enroll such a participant.

C. Id-card

This card is used to identify each study participant. Once the parents/legal guardians sign the informed consent form, a photo will be taken. Printing of the photograph will be done at the base hospital and the Id-card will be kept ready for the first vaccination day (day 1) to be given to the study participant. The card will include the unique number, the barcode number, a photo, name and address. After completing enumeration and interviews in each village, invitations will be given to the eligible girls for vaccination, indicating the date, time and venue of the vaccination clinic.

Participants must be reminded to carry their Id-card with them to help participant authentication at subsequent vaccinations and follow-up visits.

Participant's details section (Id-card)

A	Field on the form	Instructions
1	Unique number	Indicate the household number according to the defined format (11 characters): - Site: one letter to codify the study site - Group: one digit to codify the randomization group (2 or 3 doses) according to the localization - PHC: three digits to codify the Primary Health Centre (PHC) - Village: three digits to codify the village - House number: four digits to codify the house number in the village - Serial: 2 digits to identify the participant in the household
2	Last name	Indicate the last or family name of the vaccination participant.
3	First name	Indicate the first or given name of the vaccination participant.
4	Middle name	Indicate the middle name of the vaccination participant (if applicable).
5	Age	Indicate the participant's age in years.
6	Address	Indicate the address (with full details) to facilitate participant follow-up (include information such as behind the bus station, village school, near anganwadi, etc.).
7	PHC/Panchayath and Village name	Indicate the PHC/Panchayath and village name to facilitate participant follow-up.
8	Phone	Indicate the participant's phone number to facilitate follow-up of the participant.
9	Name and address of school	If the participant is attending school/college, specify the name and address of the school. If not applicable, leave this field empty.
10	Standard class	Indicate the standard class of the participant according to the list. Specify other class if required. If not applicable, leave this field empty.
11	Division	Indicate school/college division/department if applicable to facilitate the follow-up. If not applicable, leave this field empty.
12	Contact of the PI	Include the PIs/other key site staff's contact for any emergency contact.

HPV Vaccination Programme

F

Date of follow-up	Medical history *(e.g., allergies, vaccine reactions)*
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__
__/__/20__	Next follow-up: __/__/20__

HPV Vaccination Programme

A

Study No: □·□·□□□·□□□·□□□□·□□
Site Group PHC Village House Number Serial

ID CARD

B0003IDC

Age (in years): .....

Last name: .....

First name: ..... Middle name: .....

Address: .....

.....

.....

District: ..... Village: .....

Phone: 1 ..... 2 .....

New address: .....

.....

.....

District: ..... Village: .....

Phone: 1) ..... 2) .....

Name and address of school being attended: .....

.....

Standard class: ..... Division: .....

In case of emergency, please contact:
Study contact address
and phone

HPV Vaccination Programme

B

Vaccine group: ☐ 2 ☐ 3

Sero-testing group: ☐ No ☐ Yes

Vaccination:

	1st dose	2nd dose	3rd dose
Vaccine name:	GARDASIL ®	GARDASIL ®	GARDASIL ®
Date of vaccination:	__/__/20__	__/__/20__	__/__/20__
Doctor name:			
Health centre name:			
Next dose due date:	__/__/20__	__/__/20__	
Comments:			

C

Mild and moderate adverse events (occurred at home):

Describe the events	Start reaction (date and time)	Stop reaction (date and time)
	__/__/20__ ___h___	__/__/20__ ___h___
	__/__/20__ ___h___	__/__/20__ ___h___
	__/__/20__ ___h___	__/__/20__ ___h___
	__/__/20__ ___h___	__/__/20__ ___h___
	__/__/20__ ___h___	__/__/20__ ___h___
	__/__/20__ ___h___	__/__/20__ ___h___

HPV Vaccination Programme

D

Blood collection:

	Date collected:	Specimen collected	Comment
Day 1:	__/__/20__		
Month 7:	__/__/20__		
Month 12:	__/__/20__		
Month 24:	__/__/20__		
Month 36:	__/__/20__		
Month 48:	__/__/20__		
Other date:	__/__/20__		

Requested only at day 1 and months 12, 24, 36 and 48 for sero-testing group

E

Cervical Cancer Screening:

	Visit 1	Visit 2	Visit 3
Date of visit	__/__/20__		
Colposcopy:	__/__/20__		
HPR taken:	__/__/20__		
Action taken:	__/__/20__		
Appointment date:	__/__/20__		
Appointment place:	__/__/20__		
Treatment date:			
Treatment:			
Follow-up date:	__/__/20__		

Vaccination section (Id-card)

B	Field on the form	Instructions
1	Vaccine group	Indicate whether the participant is in the 2 doses or 3 doses group. Participants will be randomly selected at each cluster (village or group of villages) to provide 50% in each group.
2	Sero-testing group	Indicate whether the participant is in the sero-testing group or not. 15% of participants will be randomly selected in each cluster (village or group of villages) for blood collection.
3	Vaccine name	By default the generic name will be: "GARDASIL".
4	Date of vaccination	Record the actual date of vaccination. This date is exactly the same as the visit date.
5	Health professional's name	Record the name of the health professional who included the participant in the study.
6	Health center name	Record the name of the vaccination health center.
7	Date next dose due	Record the date foreseen for next dose. According to the group it will be in the next 2 or 6 months.
8	Comments	If applicable, record any information to help complete the participant's vaccination data.

Mild and moderate adverse events (Id-card)

C	Field on the form	Instructions
1	Describe the event	If applicable, describe the event following the discussion with the participant.
2	Start reaction date / time	If applicable for participants, indicate/estimate the date and time of the start reaction.
3	Stop reaction date / time	If applicable for participants, indicate/estimate the date and time of the stop reaction.

Blood collection section (Id-card)

D	Field on the form	Instructions
1	Date collected	If applicable, indicate the date the blood sample was collected. If not applicable, write "NA".
2	Specimen collected	If applicable for participants, indicate if the blood sample was taken. If not applicable, write "NA".
3	Comment	If applicable, record any information to help complete the participant's blood specimen data.

Cervical cancer screening section (Id-card)

E	Field on the form	Instructions
1	Date of screening	Indicate the date of the screening (dd/mm/yyyy).
2	VIA findings	Indicate the findings of the visual inspection with acetic acid (VIA). If not applicable, write "NA".
3	VILI findings	Indicate the findings of the visual inspection with Lugol's Iodine (VILI). If not applicable, write "NA".
4	Colposcopy impression	If applicable, indicate the colposcopic impression. If not applicable, write "NA".
5	Action taken	Indicate what the action was taken after the screening examination. If not applicable, write "NA".
6	Appointment date	Indicate the date of the treatment appointment (dd/mm/yyyy), if applicable.
7	Appointment place	Indicate the place of the treatment appointment (dd/mm/yyyy), if applicable
8	Treatment date	Indicate the treatment date when the participant's treatment is completed.
9	Treatment done	Indicate whether treatment has been done in the treatment clinic.
10	Follow-up date	Record the date foreseen for next follow-up date after treatment.

Follow-up section (Id-card)

F	Field on the form	Instructions
1	Date follow-up visits	Indicate the date of the follow-up visit (dd/mm/yyyy).
2	Medical history	Detail the AE, allergies or vaccine reactions and anomalies.

D. Household form

Eligible subjects will be identified by systematic household surveys in the villages selected for the study. Each household in the villages will be visited by project health workers and will be enumerated using a household form. These forms will contain, among other things, the address, name and the total number of eligible girls in the household and the household number.

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

HOUSEHOLD FORM

1	Household number: □·□·□□□·□□□·□□□□ *Site Group PHC Village House Number*	*Barcode*
2	Address details:	
3	PHC/Panchayath and Village name:	
4	Zip Code:	□□□□□□
5	Name of head of family:	
6	Total residents:	□□
7	Total female residents:	□□
8	Total female residents eligible for screening in the household *(30-59 years)*:	□□
9	Total female residents eligible for vaccination in the household *(10-18 years)*:	□□
10	Type of house: *(1: thatched; 2: tiled; 3: concrete)*	□
11	Average monthly household income *(in Rupees)*: *(1: < 2 000; 2: 2 000-4 999; 3: 5 000-9 999; 4: ≥10 000)*	□
12	Final status of completion of household form: *(1: complete details obtained; 2: partial details obtained; 3: door locked, to be revisited; 4: refused, 8: other , specify:)*	□
13	Date of enumeration: *(dd/mm/yyyy)*	__/__/20__
14	Staff Id:	□□
Data entry done:		○

Household detail

A	Field on the form	Instructions
1	Household number	Indicate the household number according to the defined format (11 characters): - Site: one letter to codify the study site - Group: one digit to codify the randomization group (2 or 3 doses) according to the localization - PHC: three digits to codify the Primary Health Centre (PHC) - Village: three digits to codify the village - House number: four digits to codify the house number in the village
2	Address details	Indicate the address (with full details) to facilitate the participant follow-up (include information such as behind the bus station, village school, near anganwadi, etc.).
3	PHC/Panchayath and Village name	Indicate the PHC/Panchayath and village name to facilitate participant follow-up.
4	Zip Code	Indicate the zip code to facilitate participant follow-up.
5	Name of head of family	Indicate the name of the head of family to facilitate house localization.
6	Total residents	Indicate the total number of permanent residents in the house (exclude temporary visitors or neighbors in the count). If the Vaccine acceptability form is completed for the same household, check if the number matches with the total number of residents Q13.
7	Total female residents	Indicate the total number of permanent female residents in the house (exclude temporary visitors or neighbors in the count).
8	Total female residents eligible for screening	Indicate the total number of permanent female residents eligible for screening (aged between 30-59 years) in the house (exclude temporary visitors or neighbors in the count).
9	Total female residents eligible for vaccination	Indicate the total number of permanent female residents eligible for vaccine (age between 10-18 years) in the house (exclude temporary visitors or neighbors in the count).
10	Type of house	Indicate the type of house according to the list (thatched, tiles, concrete).
11	Monthly income	Indicate the average monthly household income (in rupees).
12	Final status	Indicate the final status of completion of household form according to the list: complete details obtained / partial details obtained / door locked, to be revisited / refused. Specify other reason(s).
13	Date of enumeration	Indicate the date of enumeration (dd/mm/yyyy).
14	Staff Id	Indicate the Staff Id completing this questionnaire.

Each line will describe one permanent resident in the household. Temporary visitors or neighbors should not be recorded as permanent residents.
If any girls eligible for the vaccine trial are likely to stay for the entire duration of study and has parents/legal guardians to sign the informed consent form, they can be included on this form. Screening for cervical cancer may be offered to eligible visiting women to that house.

Permanent residents in the household

B	Field on the form	Instructions
1c	Serial	Indicate the family number rank. In priority record in the first lines the eligible girls first and then the mothers. This number will be used in the next form, combine with the Household number to define the ID number: ID number = Household number (11) + Serial number (2)
2c	Given name	Indicate the family member's given or first name.
3c	Middle name	Indicate the family member's middle name.
4c	Surname/Family name	Indicate the family member's family name.
5c	Sex	Indicate the family member's sex.
6c	Age	Indicate the family member's age.
7c	Eligible for vaccine	Indicate if the family member is eligible for vaccine. Rule is: sex=female and age=10-18 years
8c	Eligible for screening	Indicate if the family member is eligible for screening. Rule is: sex=female and age= 30-59 years

Permanent residents in the household

Serial	*Given name*	*Middle name*	*Surname/Family name*	*Sex* (1:M; 2:F)	*Age* (in years)	*Eligible for vaccine* (1:no; 2:yes)	*Eligible for Screening* (1:no; 2:yes)
1				☐	☐☐	☐	☐
2				☐	☐☐	☐	☐
3				☐	☐☐	☐	☐
4				☐	☐☐	☐	☐
5				☐	☐☐	☐	☐
6				☐	☐☐	☐	☐
7				☐	☐☐	☐	☐
8				☐	☐☐	☐	☐
9				☐	☐☐	☐	☐
10				☐	☐☐	☐	☐
11				☐	☐☐	☐	☐
12				☐	☐☐	☐	☐

E. Vaccination form

This form is used to document the required (regularly scheduled) vaccination visits for both 2- and 3-dose regimen through Day 1 (both groups), Day 60 (only 3-dose group), Day 180 (both groups). It is completed at each regularly scheduled vaccination visit, regardless of whether the visit is conducted within the protocol-specified window.

Note: If the immune response in the 2-dose group is less by 11% or more as compared to the 3-dose group, a decision will be taken to provide a third injection of HPV vaccine within the first year, on the conclusion that the immunogenicity associated with the two-dose regimen is inferior to that of the current standard three-dose regimen.

A. Eligibility		No	Yes
1	Has the participant any allergies to medications, food, or any vaccine?	○	○
2	Has the participant had a serious reaction after receiving any vaccination?	○	○
3	Has the participant had a health problem with asthma, heart disease, lung disease, kidney disease, metabolic disease (e.g., diabetes), epilepsy or any neurological illness, mental or physical disability or blood dyscrasia?	○	○
4	Has the participant had cancer, leukemia, AIDS, or any other immune system problem?	○	○
5	Has the participant taken cortisone, prednisone, other steroids, or anticancer drugs, or had radiation treatments in the past 3 months?	○	○
6	Has the participant any prior history of genital warts or treatment for genital warts?	○	○
7	Has the participant received a blood transfusion, any blood products, or been given a medicine called immune (gamma) globulin in the past year?	○	○
8	Has the participant undergone any surgical procedure for the removal of the uterus?	○	○
9	Is the participant married or engaged to be married in the next 6 months?	○	○
10	If the participant gets married during the vaccination period, does she refuse to use effective contraception through month 7 of the study?	○	○
11	Has the participant any plans to permanently relocate from the area prior to the completion of the study or to leave for an extended period of time when study visits would need to be scheduled?	○	○
12	Comment:		
13	**If answer is "yes" for any of these questions, participant is not eligible** Is the participant eligible to participate:	○	○

Eligibility

A	Field on the form	Instructions
1	Any allergies	Indicate whether the participant has any allergies to medications, food, or any vaccine. If yes, the participant will not be enrolled in the study.
2	Any serious reaction	Indicate whether the participant has had a serious reaction after receiving any vaccination. If yes, the participant will not be enrolled in the study.
3	Any health problem	Indicate whether the participant has had a health problem with asthma, heart disease, lung disease, kidney disease, metabolic disease (e.g., diabetes), epilepsy or any neurological illness, mental or physical disability or blood disease. If yes, the participant will not be enrolled in the study.
4	Cancer/leukemia/AIDS	Indicate whether the participant has had cancer, leukemia, AIDS, or any other immune system problem. If yes, the participant will not be enrolled in the study.
5	Any cortisone/steroids taken	Indicate whether the participant has taken cortisone, prednisone, other steroids, or anticancer drugs, or has had radiation treatments in the past 3 months. If yes, the participant will not be enrolled in the study.
6	Any genital warts	Indicate whether the participant has had any prior history of genital warts or treatment for genital warts. If yes, the participant will not be enrolled in the study.
7	Any blood transfusion	Indicate whether the participant has received a blood transfusion, any blood products, or been given a medicine called immune (gamma) globulin in the past year. If yes, the participant will not be enrolled in the study.
8	Any removal of uterus	Indicate whether the participant underwent any surgical procedure for removal of the uterus. If yes, the participant will not be enrolled in the study.
9	Married or engaged	Indicate whether the participant is married or engaged to be married in the next 6 months. If yes, the participant will not be enrolled in the study.
10	Refuse contraception use	Indicate whether the participant gets married during the vaccination period, does she refuse to use effective contraception through to month 7 of the study. If yes, the participant will not be enrolled in the study.
11	Migration	Indicate whether the participant has any plans to permanently relocate from the area prior to the completion of the study or to leave for an extended period of time when study visits would need to be scheduled If yes, the participant will not be enrolled in the study.
12	Comment	If applicable, record any information which may help to complete the participant's eligibility questions.
13	Eligibility	- If any of the previous question (1 to 12) reply is "yes", you should indicate "yes" in this field. In this case the participant will not be eligible for this study and the interview and procedure will stop at this point. - If all previous questions (1 to 12) are "negative", then the participant is eligible for the study and you will collect the consent form.

14	Consent given by parents/legal guardian	If the participant is eligible, indicate whether the the consent is given by the parents or by legal guardians If the participant is not eligible, leave this field empty.
15	Consent given by participant	If the participant is eligible, indicate whether she is giving the consent. If the participant is not eligible, leave this field empty.
16	Consent date	If the participant is eligible, indicate the consent date. If the participant is not eligible, leave this field empty.
17	Staff Id	Indicate the Staff Id completing this questionnaire.

If eligible fill consent form and proceed further

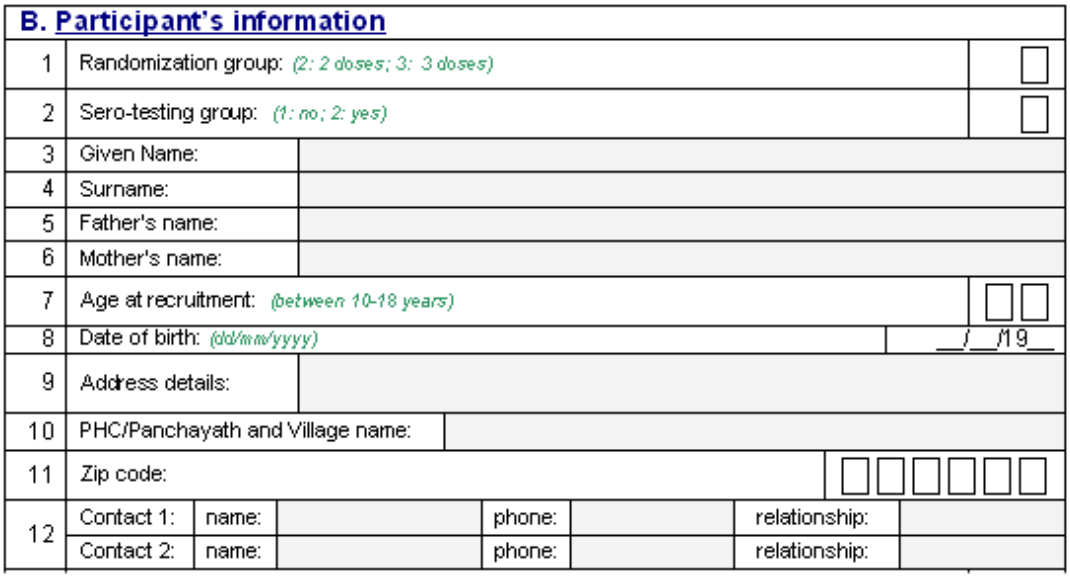
14	Consent given by parents/legal guardian: *(1: no; 2: yes)*	☐
15	Consent given by participant: *(1: no; 2: yes)*	☐
16	Consent date: *(dd/mm/yyyy)*	__/__/20__
17	Staff Id:	☐☐
Data entry done:		○

If participant is eligible according to the Eligibility table (A) you can continue to fill in the form and process for vaccination (except if there is a medical contra-indication).
If participant is not eligible stop the vaccination process and do not collect any more information.

When participant is eligible and is present during the registration for the first vaccination day, a barcode number will be associated to the participant folder.

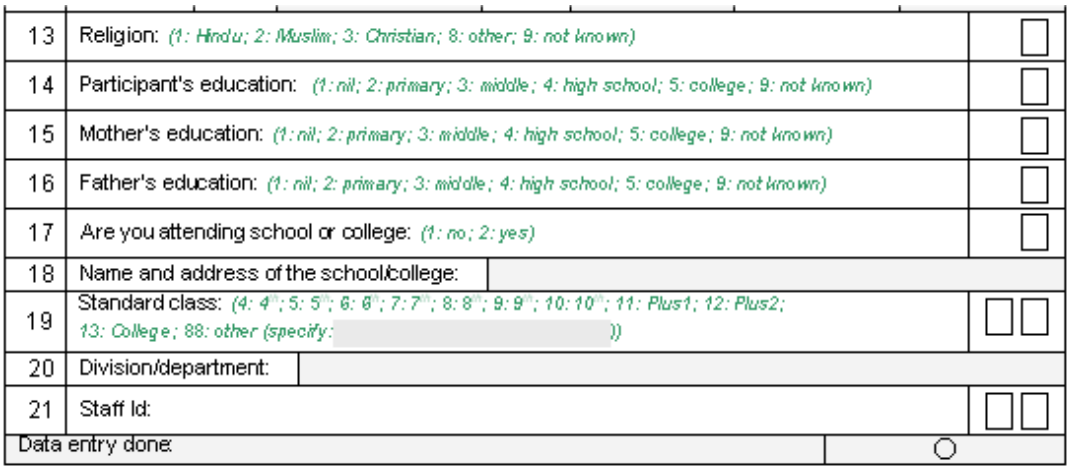
Participant information

B	Field on the form	Instructions
1	Randomization group	Indicate the study group according to the list: - to be vaccinated with 2 doses - to be vaccinated with 3 doses
2	Sero-testing group	Indicate whether the participant is in the sero-testing group or not. Participants will be randomly selected at each cluster (village or group of villages) to provide a 15% sample of girls for blood collection
3	Given Name	Indicate the given name of the vaccination participant.
4	Surname	Indicate the surname of the vaccination participant.
5	Father's name	Indicate the father's name of the vaccination participant.
6	Mother's name	Indicate the mother's name of the vaccination participant.
7	Age at recruitment	Indicate the age in years of the participant.
8	Date of birth	Indicate the date of birth of the vaccine participant. If the date of birth is not known, age estimated by the counselor will be written. They can write "30/06/YEAR" to record this information.
9	Address details	Indicate the address (with full details) to facilitate participant follow-up. To facilitate the participant follow-up, include information such as behind the bus station, village school, near anganwadi, etc.
10	PHC/Panchayath and Village name	Indicate the PHC/Panchayath and village name.
11	Zip code	Indicate the zip code to facilitate participant follow-up.
12	Contact: name/phone /relationship	Indicate at least one or two contacts (name + phone + relationship) to facilitate follow-up of the participant.



B. Participant's information							
1	Randomization group: *(2: 2 doses; 3: 3 doses)*						☐
2	Sero-testing group: *(1: no; 2: yes)*						☐
3	Given Name:						
4	Surname:						
5	Father's name:						
6	Mother's name:						
7	Age at recruitment: *(between 10-18 years)*						☐☐
8	Date of birth: *(dd/mm/yyyy)*						__/__/19__
9	Address details:						
10	PHC/Panchayath and Village name:						
11	Zip code:						☐☐☐☐☐☐
12	Contact 1:	name:		phone:		relationship:	
	Contact 2:	name:		phone:		relationship:	

13	Religion	Indicate the religion of the participant according to the list.
14	Education	Indicate the level of education of the participant according to the list.
15	Mother's education	Indicate the mother's level of education of the participant according to the list.
16	Father's education	Indicate the father's level of education of the participant according to the list.
17	Attending school/college	Indicate whether the participant is attending school or college.
18	School/college address	If the participant is attending school/college specify the name and address of the school. If not applicable, leave this field empty.
19	Standard class	Indicate the standard class of the participant according to the list. Specify other class if required. If not applicable, leave this field empty.
20	Division/department	Indicate school/college division/department if applicable to facilitate the follow-up. If not applicable, leave this field empty.
21	Staff Id	Indicate the Staff Id completing this questionnaire.

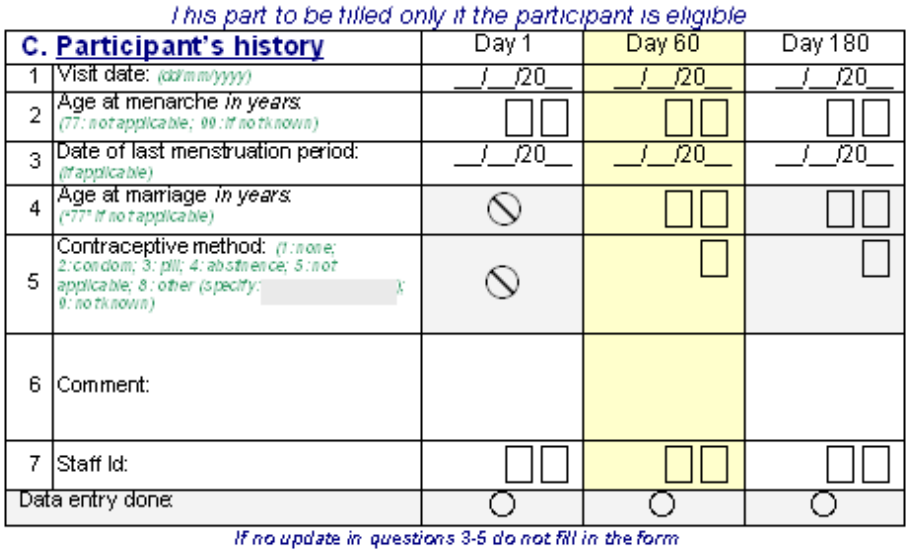


The participant history table is used to collect participant's history data. Complete data are required to facilitate participant follow-up. If a participant is being re-vaccinated, use the next column to update the last information status according to the column heading ("Day 1"; "Day 60"; "Day 180").

Attention: The column of "Day 60" should be only used for the 3 dose regimen randomized group and should be left blank for the 2 dose group according to the protocol.

Participant's history

C	Field on the form	Instructions
1	Visit date	Record the actual date of the vaccination visit.
2	Age at menarche	Indicate the age at menarche. If the participant does not know her age at menarche, try to estimate it with the participant's help. If you cannot estimate this age record the value "99" on the questionnaire associated to "not known".
3	Date of last menstruation	If applicable, indicate the date of last menstrual period.
4	Age at marriage	If applicable, indicate the age at marriage. If the marriage is recent do not forget to update the participant's update form to collect husband's name, and the new address of the participant. If not applicable, select "77" corresponding to not applicable.
5	Contraceptive method	If applicable, indicate the most frequent contraceptive method used. Specify other contraceptive method if required. If not applicable, select "7" corresponding to not applicable.
6	Comment	If applicable, record other information to help complete the participant's history data.
7	Staff Id	Indicate the Staff Id completing this questionnaire



The vital signs table is used to collect participant's vital signs data. Complete data are required to facilitate participant follow-up and to ensure eligibility to the protocol. If a participant is being re-vaccinated for the second or the third dose, use the next column to update the last vital status according to the column heading ("Day 1"; "Day 60"; "Day 180").

Attention: The column "Day 60" should be only used for the 3 dose regimen randomized group and should be left blank for the 2 dose group according to the protocol.

The "Any additional dose" column should be only used in case of protocol violation and for any visit that does not occur in the visit window of the doses (Day1, Day 60 or Month 2, Day 180 or Month 6). It will also be used if we decide to give the third dose to the participants enrolled in the 2 doses regimen according to the protocol.

When recording weight, height, temperature, blood pressure (BP), pulse, remember to use leading zeros when needed. Make sure you report the result with the correct unit for these different values (If value is 99 cm, record 099 cm to avoid confusion). Round off weight, height and temperature to the closest entire value.

D. Vital signs (vaccination day):		Day 1	Day 60	Day 180
1	Date of examination: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
2	Is the participant sick today? *(1: no; 2: yes)*	☐	☐	☐
3	Weight *(kg)*:	☐☐	☐☐	☐☐
4	Height *(cm)*:	☐☐☐	☐☐☐	☐☐☐
5	Temperature *(°F)*:	☐☐☐	☐☐☐	☐☐☐
6	BP systolic *(mm Hg)*:	☐☐☐	☐☐☐	☐☐☐
7	BP diastolic *(mm Hg)*:	☐☐☐	☐☐☐	☐☐☐
8	Pulse rate *(per min)*:	☐☐☐	☐☐☐	☐☐☐
9	Any allergic reactions/discomfort/ mild adverse reactions after previous dose of HPV vaccine? *(1: no; 2: yes)*	⊘	☐	☐
10	Any severe adverse events after prior dose of HPV vaccine? *(1: no; 2: yes)*	⊘	☐	☐
11	Clinical eligibility for vaccination: *(1: no; 2: yes; 9: not known)*	☐	☐	☐
12	Comment:			
13	Staff Id:	☐☐	☐☐	☐☐
Data entry done:		○	○	○

Vital signs

D	Field on the form	Instructions
1	Date of examination	Record the actual date of the examination visit. This date is exactly the same as that of the vaccination visit date.
2	participant sick today	Indicate whether the participant is sick today. If participant is sick, participant is not eligible and vaccination should be postponed to another day preferably within the visit window.
3	Weight	Indicate the participant's weight in kilograms.
4	Height	Indicate the participant's height in centimeters.
5	Temperature	Indicate the participant's temperature in Fahrenheit.
6	BP systolic	Indicate the participant's blood pressure systolic in mmHg.
7	BP diastolic	Indicate the participant's blood pressure diastolic in mmHg.
8	Pulse rate	Indicate the participant's pulse rate per minute.
9	Any AE	Indicate whether the participant has had any allergic reactions/discomfort/ mild adverse events (AE) after prior dose of HPV vaccine. If participant has had any serious adverse event (SAE) or anaphylactic reaction, participant is not eligible and vaccination should not be done. Vaccination should be continued in case of minor side effects/injection site side effects at the discretion of the study clinician in consultation with the site PI. Since IARC will be receiving the participant's data regularly, if any participant has suffered any serious adverse event of any adverse event for which further vaccination should be discontinued, IARC will send an email notification to the site to stop further vaccination. Summary of the AEs from all the sites will be regularly distributed to inform the sites. Safety calls of all sites PIs/Co-PIs will be organized to discuss AEs.
10	Any SAE	Indicate whether the participant had any serious adverse events (SAE) after prior dose of HPV vaccine. If participant has any SAE, participant is not eligible and vaccination should not be given.
11	Clinical eligibility for vaccination	Indicate whether the participant is eligible for vaccination. If participant is not eligible, no vaccination should be done.
12	Comment	If applicable, record any information to help complete the participant's vital signs data (especially the non eligibility reason(s).
13	Staff Id	Indicate the Staff Id completing this questionnaire.

A urine pregnancy test should be done for the married women or if indicated in case of amenorrhea.

This urine pregnancy test table is used to document laboratory results of urine specimens collected before the vaccination. Record urine specimen results on this form as they become available. If a urine pregnancy test is not done or not collected, mark the "not done" option in item 2. Once a participant tests positive for HCG urine pregnancy and a pregnancy form has been completed for this pregnancy, subsequent positive pregnancy test results should not be recorded on this form unless they represent a new pregnancy.

Participant with a positive urine pregnancy test result should be excluded from the study and from receiving any further vaccine dose at any time point. Indeed, the protocol requires avoiding pregnancy while participants receive the 2- or 3- dose vaccine course, so each pregnant girl should be excluded from the trial.

Urine pregnancy test

E	Field on the form	Instructions
1	Test date	Record the actual date of the urine test. This date is exactly the same as that of the vaccination visit date.
2	Urine pregnancy test result	Indicate the participant's urine pregnancy test result.
3	Comment	If applicable, record all proper information to help complete the participant's urine pregnancy test and specify the reason(s) why the required pregnancy test was not done, if applicable.

E. Urine pregnancy test: *Married women only or if indicated in case of amenorrhea*		**Test 1**	**Test 2**	**Test 3**	**Test 4**
1	Test date: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__	__/__/20__
2	Urine pregnancy test result: *(1: negative; 2: positive; 3: not done)*	☐	☐	☐	☐
3	Comment:				
Data entry done:		○	○	○	○

At Day 1, blood samples are collected only from the sero-testing group (15%) for both 2 and 3 doses regimen. This table should be kept blank for the participants not included in the sero-testing group. This table should not be used for month 2 or month 6 visits.

Blood collection

F	Field on the form	Instructions
1	Specimen collected	If applicable (day 1 only) for sero-testing group participants, indicate if the blood sample is taken. This is not required for other participants, since this form is to be completed only for the sero-testing group on Day 1.
2	Reason not collected	If applicable and negative reply to the previous question, give the main reason (see below the table for the codes: refused, lost to follow-up, technical difficulty, withdrew consent, specify other reason if required). If not applicable, leave this field empty.
3	Date specimen collected	If applicable, indicate the date of blood sample collected. If not applicable, leave this field empty.
4	Staff Id	Indicate the Staff Id completing this questionnaire.

F. Blood collection: (only for sero-testing group)		Day 1
1	Specimen collected: *(1: no; 2: yes)*	☐
2	Reason not collected: *(1: technical difficulty; 2: refused; 3: missing; 8: other reason (specify:))*	☐
3	Date specimen collected: *(dd/mm/yyyy)*	__/__/20__
4	Staff Id in the field clinic:	☐☐
Data entry done:		○

If participant is eligible according to the Eligibility table (A) and if there is no contra-indication(s) in the vital status table (D) you can fill in this table and vaccinate.
If participant is not eligible leave this table empty and do not vaccinate her.

Vaccination record

G	Field on the form	Instructions
1	Date of vaccination	Record the actual date of vaccination. This date is exactly the same as the visit date.
2	Place of vaccination	Indicate where vaccination was carried out according to the list. Specify other place(s) if required.
3	Injection site	Indicate the injection site according to the list. Specify other injection site(s) if required.
4	AE after injection	Indicate the adverse event allergic reaction/discomfort 30 minutes after injection.
5	Comments	If applicable, record any other information to help complete the participant's vaccination record.
6	Staff Id	Indicate the Staff Id completing this questionnaire.

G. Vaccination record:		Day 1	Day 60	Day 180
1	Date of vaccination: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
2	Place of vaccination: *(1 base hospital; 2: PHC; 3: field clinic; 4: school; 5: home; 8: other (specify:))*	☐	☐	☐
3	Injection site: *(1: left arm, 2: right arm, 3: left thigh, 4: right thigh, 5: left gluteal, 6: right gluteal, 8: other(specify:))*	☐	☐	☐
4	Allergic reaction/discomfort 30 min after injection: *(1: no; 2: yes; 9: not known)*	☐	☐	☐
5	Comments:			
6	Staff Id:	☐☐	☐☐	☐☐
Data entry done:		○	○	○

Guidelines for pre-vaccination signs and symptoms

If any of the following signs and symptoms occur during the medical examination, vaccination should be postponed to another day preferably within the visit window.

Following signs or symptoms the day of the clinical examination:

- **Hypersensitivity**, including serious allergic reactions to yeast (vaccine component)
- **Fever** (>100º F)
- **Infectious disease** at the time of vaccination requiring use of antibiotics

After a previous Gardasil dose:

- **Severe reaction**
- Signs of an **allergic reaction** (difficulty breathing, wheezing (bronchospasm), hives, rash)

F. Participant update during vaccination/follow-up form

PARTICIPANT UPDATE DURING VACCINATION/FOLLOW-UP

Id number:	□·□·□□□·□□□·□□□□·□□	Barcode
	Site Group PHC Village House Number Serial	

The participant/update form is used to collect participant demographic and socioeconomic changed data. Complete data is required to facilitate participant follow-up and future contacts. If a participant is being re-vaccinated or followed-up a new time, use the next column to update the previous information status.

	A. Participant update:	Update 1	Update 2	Update 3
1	Date: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
2	Source of information: *(1: household visit; 2: field clinic; 3: follow-up visit; 4: marriage invitation letter; 5: phone call; 6: letter; 8: other (specify))*	□	□	□
3	Vital status: *(1: alive; 2: dead; 9: not known)*	□	□	□
4	Date of death:	__/__/20__	__/__/20__	__/__/20__
5	If dead, cause of death:			
6	Marital status: *(1: unmarried; 2: married; 3: widowed; 4: separated; 8: other; 9: not known)*	□	□	□
7	Date of marriage:	__/__/20__	__/__/20__	__/__/20__
8	Husband's name:			
9	Migration status: *(1: migrated; 2: not migrated; 9: unknown)*	□	□	□
10	Migration date: *(if applicable)*	__/__/20__	__/__/20__	__/__/20__
11	New Address details:			
12	New village/city:			
13	New zip code:	□□□□□□	□□□□□□	□□□□□□
14	New contact name: phone no: Relationship:			
15	Completed 18 years of age: *(1: no; 2: yes)*	□	□	□
16	If yes, new consent signed? *(1: no; 2: yes)*	□	□	□
17	Date of last menstrual period: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
18	Contraceptive method: *(1: none; 2: condom; 3: pill; 4: sterilisation; 5: IUD; 6: abstinence; 7: not applicable; 8: other (specify:); 9: not known)*	□	□	□
19	Pregnancy: *(1: no; 2: yes; 9: not known)*	□	□	□
20	Date of delivery: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__
21	Comment:			
22	Staff Id:	□□	□□	□□
	Data entry done:	○	○	○

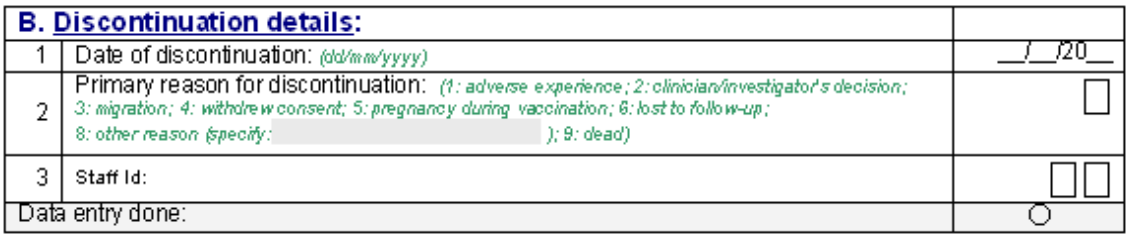
Participant update

C	Field on the form	Instructions
1	Date	Record the actual date of data update collection.
2	Source of information	If any change, indicate the source of information. Specify other source of data.
3	Vital status	Indicate if the participant is alive/dead. If dead, give date of death.
4	Date of death	Record the actual date of death. When possible, record the participant's complete death date (day, month, year). If the contact does not know the participant's date of death, try to estimate the best approximate date with the contact. Do not record a partial date of death, this may generate errors. Specify in the comments field that the date of death is estimated and try to receive an official death certificate as soon as possible to complete the participant's file. If the death is linked with the clinical trial, please collect all participant's history and/or adverse events on the serious adverse events form.
5	Cause of death	If applicable, specify the cause of death.
6	Marital status	If any change, indicate the marital status. Select "unmarried" for "single", and "separated" for "divorced".
7	Date of marriage	If any change, record the date of marriage. When possible, record the participant's complete marriage date (day, month, year). If the participant does not know her complete date of marriage, try to estimate with the participant's help the best approximate date. Do not record a partial date of marriage this may generate errors. Specify in comment field that the marriage date is estimated. In addition, when getting married, participants will be requested to send their marriage invitation letter to the project and to register their post marriage address details to facilitate follow-up after marriage.
8	Husband's name	If any change, indicate the name of the girl's husband for married girls.
9	Migration status	If any change, indicate the marital status.
10	Migration date	If any change and if the participant migrated (previous question), then indicate the date of migration. When possible, record the participant's complete migration date (day, month, year). If the participant does not know her complete date of migration, try to estimate with the participant's help the best approximate date. Do not record a partial date of migration this may generate errors. Specify in comment field that the migration date is estimated.
11	Address	If any change, indicate the new address (with full details) to facilitate participant follow-up.
12	Village/city	If any change, indicate the new village/city to facilitate participant follow-up.
13	Zip code	If any change, indicate the new zip code to facilitate participant follow-up.
14	Contact name / Phone no / Relationship	If any change, indicate the new contact name, phone number and relationship to facilitate participant follow-up.
15	Attained 18 years of age	Indicate if the participant has reached the age of 18..
16	New consent signed	If the participant is older than 18 years then she must sign a new consent form. So, if applicable, indicate whether this new consent form was signed. Do not forget to put a copy of the new consent form in the participant's file for our archives.
17	Date of last menstrual period	If applicable, indicate the date of last menstrual period.
18	Contraceptive method	If applicable, indicate the most frequent contraceptive method used. Specify other contraceptive method if required. If not applicable, select "7" corresponding to not applicable.
19	Pregnancy	If any change and if applicable indicate whether the participant is pregnant. If yes, remind her to inform us when delivered or any problem during pregnancy.
20	Date of delivery	If applicable, indicate the date of the last delivery.
21	Comment	If applicable, record as much information as possible to help to follow-up this participant.
22	Staff Id	Indicate the Staff Id completing this questionnaire

The discontinuation form is completed for every enrolled participant either at the scheduled exit/end of study visit or when the participant is no longer participating in the study. A complete date is required, unless termination is due to death.

Discontinuation

B	Field on the form	Instructions
1	Date of discontinuation	Date the site determined that the participant was no longer in the study
2	Primary reason for discontinuation	Although more than one of the listed reasons for discontinuation may describe why a participant left the study early, select only the primary reason for discontinuation. If an adverse experience is selected, record the date on which the AE was recorded. In situations where more than one AE is associated with discontinuation, record the AE that most strongly influenced the decision to terminate. If a participant experiences any SAE after the first or second dose and next dose is canceled as per investigator's/IARC's decision, she should be followed-up till the end of the study with regular blood draw and collection of cervical cells following 18 months of marriage/6 months of delivery.
3	Staff Id	Indicate the Staff Id completing this questionnaire.



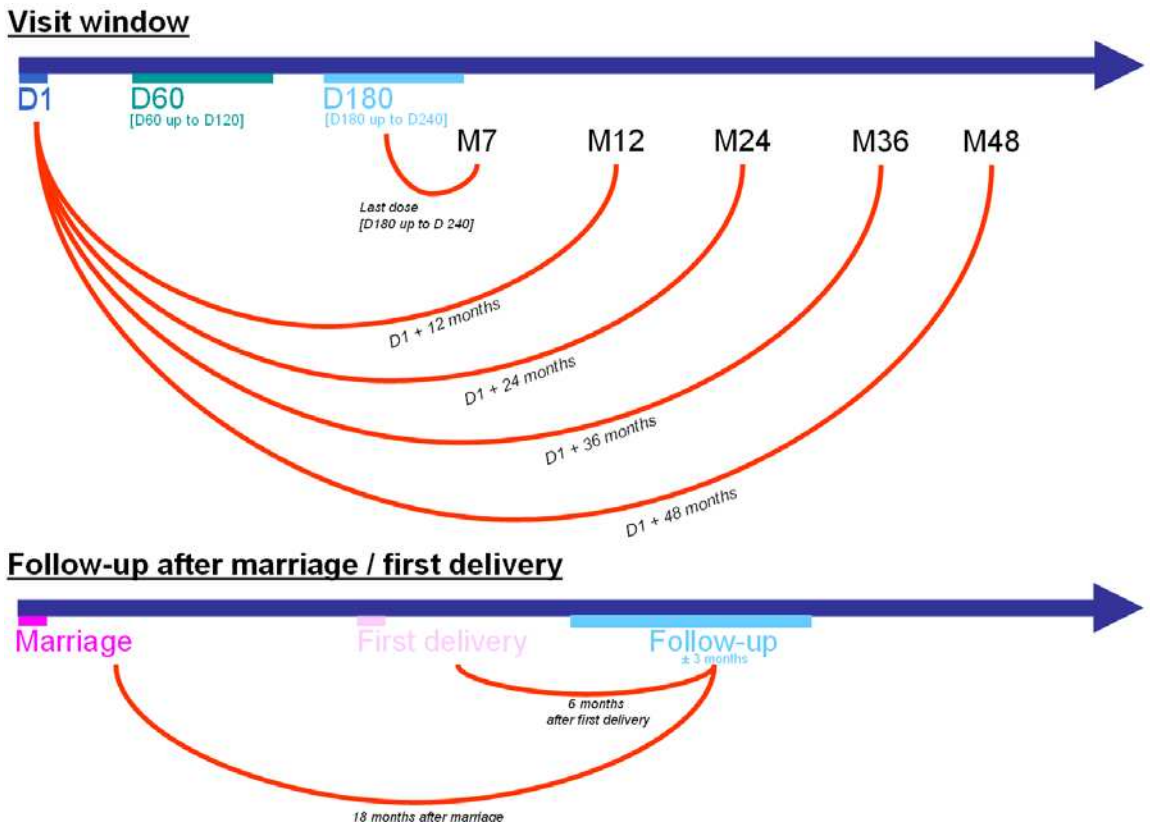
B. Discontinuation details:		
1	Date of discontinuation: *(dd/mm/yyyy)*	__/__/20__
2	Primary reason for discontinuation: *(1: adverse experience; 2: clinician/investigator's decision; 3: migration; 4: withdrew consent; 5: pregnancy during vaccination; 6: lost to follow-up; 8: other reason (specify:); 9: dead)*	☐
3	Staff Id:	☐☐
Data entry done:		○

G. Follow-up form

This form is used to document the required (regularly scheduled) follow-up visits through months 7 to 48. It is completed at each scheduled follow-up visit, at months 7, 12, 24, 36 and 48.

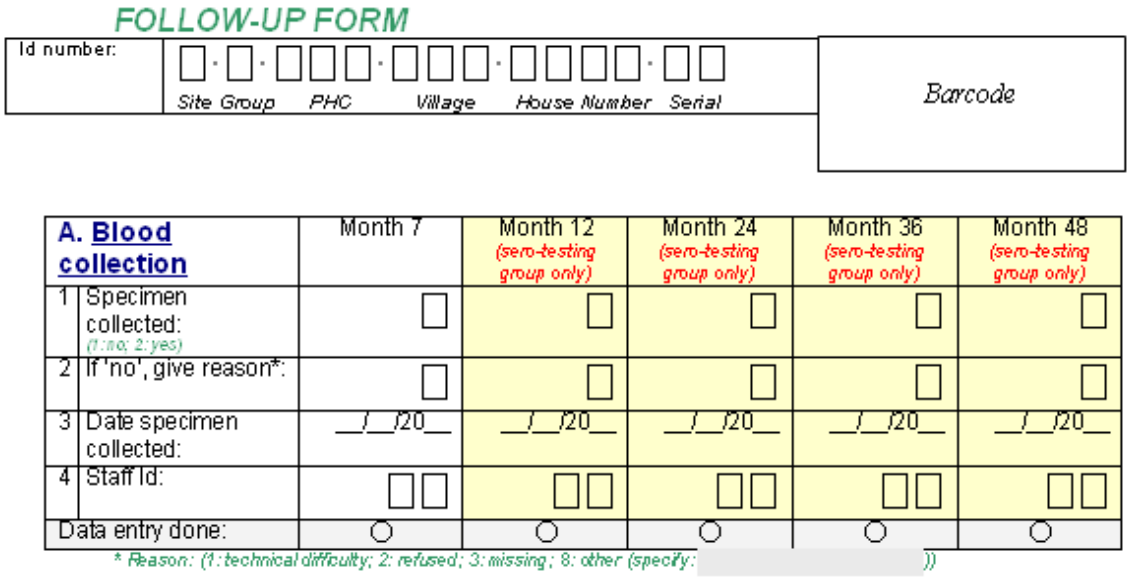
- Follow-up dates are calculated according to the day 1 date except for the month 7, which is based on the last dose date (day 180 + 2 months window).
  So, ideally if date of last dose is day 180, first follow-up will be at day 210,
  but if date of last dose is at day 240, first follow-up (M7) will be day 270.
  In all other case follow-up at 12 months (24, 36 and 48) will be based on the first day, although doses are delayed.
- Once the girl gets married, cervical cells will be collected from her 18 months after marriage or 6 months after the first delivery and then yearly thereafter. Within a 3-month window this yearly follow-up visit could be combined with the vaccine follow-up visit. In other cases follow-up visits will be conducted in addition to the yearly vaccine follow-up visit.

- At month 7, blood samples are collected for all participants.
- At months 12, 24, 36 and 48, blood samples are only collected for sero testing group (15% of participants).



Blood collection

C	Field on the form	Instructions
1	Specimen collected	If applicable (month 7 for all participants and months 12, 24, 36 and 48 only for sero testing group), indicate if the blood specimen is collected. If not applicable (month 12, 24, 36 and 48 for non sero testing group), leave this field empty.
2	If 'no' give reason	If applicable and negative reply to question 1 above, give the main reason (see the table below for the codes: refused, lost to follow-up, technical difficulty, withdrew consent, specify other reason if required). If not applicable, mention "NA".
3	Date specimen collected	If applicable, indicate the date of specimen collected. If not applicable, leave this field empty.
4	Staff Id	Indicate the Staff Id completing this questionnaire.



A. Blood collection		Month 7	Month 12 (sero-testing group only)	Month 24 (sero-testing group only)	Month 36 (sero-testing group only)	Month 48 (sero-testing group only)
1	Specimen collected: (1:no; 2:yes)	☐	☐	☐	☐	☐
2	If 'no', give reason*:	☐	☐	☐	☐	☐
3	Date specimen collected:	__/__/20__	__/__/20__	__/__/20__	__/__/20__	__/__/20__
4	Staff Id:	☐☐	☐☐	☐☐	☐☐	☐☐
Data entry done:		○	○	○	○	○

* Reason: (1: technical difficulty; 2: refused; 3: missing; 8: other (specify:))

Speculum examination is done 6 months after the first delivery and at yearly intervals, and for married women after 18 months. If not applicable, do not fill-in this part.

Speculum examination

D	Field on the form	Instructions
1	Date of examination	Indicate the date of examination.
2	Speculum examination done	Indicate if a speculum examination is done. Specify other reason if required.
3	Cervical cells collected	Indicate if the specimen is taken.
4	HC2 / Fast HPV	Indicate the HC2 / Fast HPV result, if applicable.
5	Action	Indicate the action taken after the update of the tests, if applicable.
6	Staff Id	Indicate the Staff Id completing this questionnaire

Part B for women 6 months after first delivery and at yearly intervals; for married women after 18 months

B. Speculum examination*		Exam. 1	Exam. 2	Exam. 3	Exam. 4
1	Date of examination: (dd/mm/yyyy)	__/__/20__	__/__/20__	__/__/20__	__/__/20__
2	Speculum examination done: (1: no, 2: yes; 3: not cooperative;; 8: other:)	☐	☐	☐	☐
3	Cervical cells collected: (1: no; 2: yes)	☐	☐	☐	☐
4	HC2 / Fast HPV: (1: negative; 2: positive; 3 specimen damaged/lost; 9: not known)	☐	☐	☐	☐
5	Action: (1: reassurance; 2: referral for colposcopy; 3: lost to follow-up; 9: not known)	☐	☐	☐	☐
6	Staff Id:	☐☐	☐☐	☐☐	☐☐
Data entry done:		○	○	○	○

** If PCR+ or HPV+ proceed to colposcopy*

H. Diagnostic investigation form for HPV+ participants

For who?

Vaccinated girls
Cervical cells will be collected for HPV testing and typing from the participants **6-months after their first delivery** and once a year thereafter. HPV testing and typing of the collected cervical cells will be carried out in a central laboratory in India using standard methodology. Women positive on HPV testing will be advised colposcopy and directed biopsies, depending on colposcopic findings.

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

DIAGNOSTIC INVESTIGATION FORM FOR HPV+ PARTICIPANTS

Id number:	□·□·□□□·□□□·□□□□·□□	Barcode
	Site Group PHC Village House Number Serial	

		Visit 1	Visit 2	Visit 3	Visit 4
1	Date of examination: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__	__/__/20__
2	Reason for examination: *(1: HPV+; 2: gyn. Symp.; 8: other:)*	□	□	□	□
3	Reid score:	□	□	□	□
4	Colposcopy diagnosis: *(1: normal cervix, 2: inflammation; 3: probable low grade disease (CIN 1/ atypia, HPV infection); 4: probable high grade disease (CIN 2/3 or CIS); 5: probable glandular lesion, 6: preclinical invasive cancer, 7: frank invasive cancer; 8: unsatisfactory colposcopy, 9: not done)*	□	□	□	□
5	Biopsy taken: *(1: no; 2: yes)*	□	□	□	□
6	Reason biopsy not done: *(1: refused; 2: lost to follow-up; 3: technical difficulty; 8: other reason (specify:))*	□	□	□	□
7	Histopathology report: *(01: normal cervix; 02: inflammation; 03: atypia; 04: CIN 1; 05: CIN 2; 06: CIN 3; 07: adenocarcinoma in-situ; 08: micro invasive carcinoma; 09: invasive squamous cell carcinoma; 10: invasive adenocarcinoma; 11: other carcinoma (specify:); 88: other (specify:); 13: inadequate/ inconclusive biopsy; 14: biopsy not done)*	□□	□□	□□	□□
8	Final diagnosis: *(1: normal; 2: CIN 1; 3: CIN 2; 4: CIN 3; 5: adenocarcinoma in situ; 6: invasive cancer; 9: not known)*	□	□	□	□
9	Action taken *(1: reassured; 2: referred for treatment; 8: other (specify:))*	□	□	□	□
10	Treatment date: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__	__/__/20__
11	Type of treatment: *(0: refused treatment; 1: cryotherapy; 2: cold coagulation; 3: LEEP; 4: conization; 5: hysterectomy; 6: anti-cancer treatment; 8: other (specify:))*	□	□	□	□
12	Staff Id:	□□	□□	□□	□□
Data entry done:		○	○	○	○

Screening

C	Field on the form	Instructions
1	Date of examination	Indicate the date of examination (dd/mm/yyyy).
2	Reason for examination	Indicate the reason for examination according to the list. Specify other contraceptive method if required.
3	Reid score	Indicate the Reid score. Check the guidelines for completing the Reid Score Index (RCI).
4	Colposcopy diagnosis	If applicable, indicate the colposcopic diagnosis.
5	Biopsy taken	If applicable, indicate whether a biopsy was taken or not.
6	Reason biopsy not done	If applicable, if biopsy was not taken, give the reason why according to the list. Specify other reason(s), if required.
7	Histopathology report	If applicable, indicate when you receive the laboratory histopathology report. Specify other carcinoma or other pathology if required.
8	Final diagnosis	If applicable, specify the final the diagnosis according to colposopy/histopathology report.
9	Action taken	If applicable, specify the action taken according to the final diagnosis.
10	Treatment date	If applicable, indicate the treatment date (dd/mm/yyyy).
11	Treatment type	If applicable, indicate the treatment given. Specify other treatment if required.
12	Staff Id	Indicate the Staff Id completing this questionnaire.

I. Screening of mothers

For who?

Girls' mothers
As a complimentary strategy, **50% of the girls' mothers** will be offered cervical screening during the first month of vaccination clinic using visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) followed by colposcopy, directed biopsy and treatment by cryotherapy/LEEP. The **remaining 50% of the mothers** will be offered screening during the last month of the vaccination clinic.

Participant information

A	Field on the form	Instructions
1	Id number	Indicate the Id Number and stick the barcode associated with this form.
2	Given Name	Indicate the given (or first) name of the screening participant.
3	Surname	Indicate the surname (or last name) of the screening participant.
4	Age at screening	Indicate the age of the screening participant (in year).
5	Address details	Indicate the address (with full details) to facilitate the participant follow-up.
6	PHC/Panchayath and Village name	Indicate the PHC/Panchayath and village name to facilitate participant follow-up.
7	Contact: name/phone /relationship	Indicate at least one or two contacts (name + phone + relationship) to facilitate follow-up of the participant.
8	Staff Id	Indicate the Staff Id completing this questionnaire.

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

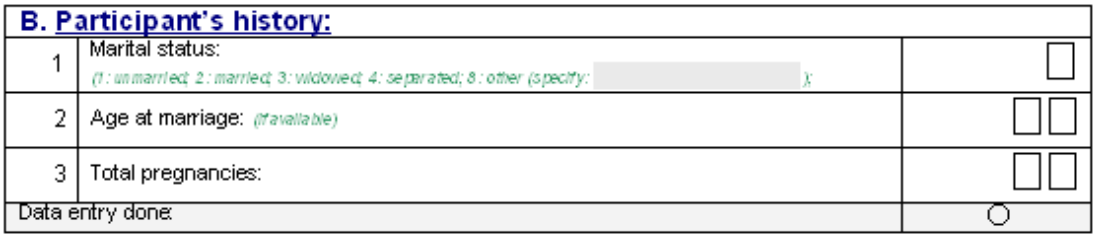
SCREENING OF MOTHERS

Barcode

A. Participant's information						
1	Id number:	☐·☐·☐☐☐·☐☐☐·☐☐☐☐·☐☐ (Site Group PHC Villag House Number Serial)				
2	Given Name:					
3	Surname:					
4	Age:	☐☐				
5	Address details:					
6	PHC/Panchayath and Village name:	/				
7	Contact 1:	name:		phone:		relationship:
	Contact 2:	name:		phone:		relationship:
8	Staff Id:	☐☐				
Data entry done:		○				

Participant history

B	Field on the form	Instructions
1	Marital status	Indicate the marital status. Select “unmarried” for “single”, and “separated” for “divorced”.
2	Age at marriage	Indicate the age at marriage. If the participant does not know her age at marriage, try to estimate with the participant the most accurate age. If you cannot estimate this age record the value “99” on the questionnaire associated to “not known”.
3	Total pregnancies	Assign a number to each infant if applicable. If none, assign the value “0”.



Screening

C	Field on the form	Instructions
1	Date of examination	Indicate the date of examination (dd/mm/yyyy).
2	Can you see the SCJ	Indicate whether the squamo-columnar junction is seen or not according to the list.
3	Findings of VIA	Indicate the findings of the visual inspection with acetic acid (VIA).
4	Findings of VILI	Indicate the findings of the visual inspection with Lugol's Iodine (VILI).
5	Reid score	Indicate the Reid score. Check the guidelines for completing the Reid Score Index (RCI).
6	Colposcopy diagnosis	If applicable, indicate the colposcopic diagnosis.
7	Biopsy taken	If applicable, indicate whether a biopsy was taken or not.
8	Histopathology report	If applicable, indicate when you receive the laboratory histopathology report. Specify other carcinoma or other pathology if required.
9	Final diagnosis	If applicable, specify the final the diagnosis according to colposopy/histopathology report.
10	Action taken	If applicable, specify the action taken according to the final diagnosis.
11	Treatment date	If applicable, indicate the treatment date (dd/mm/yyyy).
12	Treatment	If applicable, indicate the treatment given. Specify other treatment if required.
13	Staff Id	Indicate the Staff Id completing this questionnaire.

C. Screening:

1	Date of screening: *(dd/mm/yyyy)*	__/__/20__
2	Can you see the SCJ: *(1: fully visible; 2: partially visible; 3: not visible)*	☐
3	Findings of VIA*: *(1: not done; 2: negative; 3: positive; 4: suspicious for cancer)*	☐
4	Findings of VILI*: *(1: not done; 2: negative; 3: positive; 4: suspicious for cancer)*	☐
5	Reid score:	☐
6	Colposcopy diagnosis: *(1: normal cervix, 2: Inflammation; 3: probable low grade disease (CIN 1/ atypia, HPV infection); 4: probable high grade disease (CIN 2/3 or CIS); 5: probable glandular lesion, 6: preclinical invasive cancer, 7: frank invasive cancer; 8: unsatisfactory colposcopy, 9: not done)*	☐
7	Biopsy taken: *(1: no; 2: yes)*	☐
8	Histopathology report: *(01: normal cervix; 02: Inflammation; 03: atypia; 04: CIN 1; 05: CIN 2; 06: CIN 3; 07: adenocarcinoma in-situ; 08: micro invasive carcinoma; 09: invasive squamous cell carcinoma; 10: invasive adenocarcinoma; 11: other carcinoma (specify:); 88: other (specify:); 13: Inadequate/ inconclusive biopsy; 14: biopsy not done)*	☐☐
9	Final diagnosis: *(1: normal; 2: CIN 1; 3: CIN 2; 4: CIN 3; 5: adenocarcinoma in situ; 6: invasive cancer; 9: not known)*	☐
10	Action taken *(1: reassured; 2: referred for treatment; 8: other (specify:))*	☐
11	Treatment date: *(dd/mm/yyyy)*	__/__/20__
12	Treatment: *(01: cryotherapy; 02: LEEP; 03: conization; 04: hysterectomy; 05: radiotherapy only; 06: chemotherapy only; 07: radiotherapy and chemotherapy; 08: surgery+RT; 09: surgery +RT + chemotherapy; 88: other (specify:); 11: no treatment)*	☐☐
13	Staff Id:	☐☐
Data entry done:	○	

Guidelines for completing Reid colposcopic index

Colposcopic signs	Zero point	One point	Two points
Colour	Low-intensity acetowhitening (not completely opaque); indistinct acetowhitening; transparent or translucent acetowhitening Acetowhitening beyond the margin of the transformation zonePure snow-white colour with intense surface shine	Intermediate shade - grey/white colour and shiny surface (most lesions should be scored in this category)	Dull, opaque, oyster white; grey
Lesion margin and surface configuration	Microcondylomatous or micropapillary contour[1] Flat lesions with indistinct margins Feathered or finely scalloped margins Angular, jagged lesions[3] Satellite lesions beyond the margin of the transformation zone	Regular-shaped, symmetrical lesions with smooth, straight outlines	Rolled, peeling edges[2]Internal demarcations between areas of differing colposcopic appearance- a central area of high-grade change and peripheral area of low-grade change
Vessels	Fine/uniform-calibre vessels[4]- closely and uniformly placed Poorly formed patterns of fine punctation and/or mosaic Vessels beyond the margin of the transformation zone Fine vessels within microcondylomatous or micropapillary lesions[6]	Absent vessels	Well defined coarse punctation or mosaic, sharply demarcated[5] - and randomly and widely placed
Iodine staining	Positive iodine uptake giving mahogany-brown color Negative uptake of insignificant lesion, i.e., yellow staining by a lesion scoring three points or less on the first three criteria Areas beyond the margin of the transformation zone, conspicuous on colposcopy, evident as iodine-negative areas (such areas are frequently due to parakeratosis)[7]	Partial iodine uptake - variegated, speckled appearance	Negative iodine uptake of significant lesion, i.e., yellow staining by a lesion already scoring four points or more on the first three criteria

* Colposcopic grading performed with 5% aqueous acetic acid and Lugol's iodine solution. (See Appendix 3 for recipes for 5% acetic acid and for Lugol's iodine solution).
1 Microexophytic surface contour indicative of colposcopically overt cancer is not included in this scheme.
2 Epithelial edges tend to detach from underlying stroma and curl back on themselves. Note: Prominent low-grade lesions often are overinterpreted, while subtle avascular patches of HSIL can easily be overlooked.
3 Score zero even if part of the peripheral margin does have a straight course.
4 At times, mosaic patterns containing central vessels are characteristic of low-grade histological abnormalities. These low-grade-lesion capillary patterns can be quite pronounced. Until the physician can differentiate fine vascular patterns from coarse, overdiagnosis is the rule.
5 Branching atypical vessels indicative of colposcopically overt cancer are not included in this scheme.
6 Generally, the more microcondylomatous the lesion, the lower the score. However, cancer also can present as a condyloma, although this is a rare occurrence.
7 Parakeratosis: a superficial zone of cornified cells with retained nuclei.

Colposcopic prediction of histologic diagnosis using the Reid Colposcopic Index (RCI)

RCI (overall score)	Histology
0 - 2	Likely to be CIN 1
3 - 4	Overlapping lesion: likely to be CIN 1 or CIN 2
5 - 8	Likely to be CIN 2-3

J. Pregnancy events form

General instructions for the completion of the pregnancy events form

The pregnancy events form is used to document all pregnancies reported in this clinical trial. This form will be used to document maternal pregnancy history, fetal/infant history from previous pregnancies, and final status of the current reported pregnancy.

Pregnancies **should be reported** on these pages and not on the adverse events forms. However, **complications** during the current pregnancy may be reported on the adverse event form. This form is completed when information about a pregnancy outcome becomes available to study staff.

- All pregnancies reported during the first year of study initiation of the vaccine clinical trial should be reported directly to the sponsor (IARC) within 24 hours of the clinical site being notified of the event.
- Any pregnancy events occurring during the second, third and later years of the study will be reported on a monthly basis, except in case of anomalies.

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

PREGNANCY EVENTS

Id number:	☐·☐·☐☐☐·☐☐☐·☐☐☐☐·☐☐	Barcode
	Site Group PHC Village House Number Serial	

		1	2	3	4
1	Date of delivery/termination: *(dd/mm/yyyy)*	__/__/20__	__/__/20__	__/__/20__	__/__/20__
2	Place of delivery: *(1: home; 2: PHC; 3: hospital)*	☐	☐	☐	☐
3	Antenatal events: *(1: uneventful; 2: pre-eclampsia; 3: gestational diabetes; 4: placenta previa; 5: molar pregnancy; 6: fetal distress; 7: multiple gestation; 8: premature delivery; 9: other (specify:))*	☐	☐	☐	☐
4	Pregnancy outcome: *(1: full term normal delivery; 2: spontaneous abortion; 3: elective abortion; 4: still birth; 5: neonatal death)*	☐	☐	☐	☐
5	If live birth, type of delivery: *(1: vaginal; 2: caesarean section; 8: other (specify:); 9: not known)*	☐	☐	☐	☐
6	If applicable, reason for caesarean section: *(1: fetal distress; 2: failure to progress; 3: cephalopelvic disproportion; 4: breech/mal presentation; 5: placenta previa/cord prolapse; 6: multiple gestations; 9: not known)*	☐	☐	☐	☐
7	Number of babies:	☐	☐	☐	☐
8	Weight of the infant in Kg (*lowest if multiple*):	☐·☐	☐·☐	☐·☐	☐·☐
9	Infant outcome: *(1: normal; 2: premature; 3: congenital anomaly; 8: other (specify:); 9: not known)*	☐	☐	☐	☐
10	If congenital anomaly present, indicate the type of anomaly: *(see behind for code)*	☐☐☐	☐☐☐	☐☐☐	☐☐☐
11	Post natal events *(1: uneventful; 2: bleeding; 3: retained placenta; 4: septicemia; 5: hysterectomy; 8: other (specify:); 9: not known)*	☐	☐	☐	☐
12	Breast feeding given: *(1: no; 2: yes)*	☐	☐	☐	☐
13	Post natal contraception followed: *(1: no; 2: yes)*	☐	☐	☐	☐
14	Remarks:				
15	Staff Id:	☐☐	☐☐	☐☐	☐☐
Data entry done:		○	○	○	○

Pregnancy outcome

	Field on the form	Instructions
1	Date of delivery/termination	Record the actual date of delivery for a "live birth" infant, or for a "fetal loss" or for a neonatal death
2	Place of delivery	Indicate the place of delivery according to the list
3	Antenatal events	Indicate the antenatal events. Specify other, if necessary
4	Pregnancy outcome	Indicate the pregnancy outcome
5	Type of delivery	Indicate the delivery method used for this infant/fetus. Specify other, if necessary
6	Reason for caesarean section	If caesarean section was the method of delivery, indicate the reason
7	Number of babies	Assign a number to each infant, if applicable
8	Weight of the infant	Indicate the birth weight, if applicable. If the birth weight is recorded in pounds and ounces, convert completely in kg before recording on the form. Indicate the lowest weight in case of multiple delivery
9	Infant outcome	Indicate the infant outcome, if applicable, to the question whether the infant is/was developmentally normal at the time of the delivery or termination. Specify other reason(s), if necessary. If a congenital anomaly is identified, do not complete the adverse event form. A congenital anomaly is not considered an adverse event of the mother (study participant)
10	Indicate the type of anomaly	If applicable, indicate the type of anomaly according to the listing of congenital anomalies
11	Post natal events	Indicate the post natal events. Specify other reason(s). if necessary
12	Breast feeding given	Indicate the fetal outcome, if applicable. Record only one category for the fetal outcome. Specify other reason(s), if necessary. If a congenital anomaly is identified, do not complete the adverse event form. A congenital anomaly is not considered an adverse event of the mother (study participant)
13	Post natal events	Indicate the post natal events. Specify other reason(s). if necessary
14	Remarks	Indicate any remark related to this pregnancy
15	Staff Id	Indicate the Staff Id completing this questionnaire

Listing of congenital anomalies

A00	***Abdominal wall defect***	
A01		***Exomphalos***
A02		***Hernia, congenital***
B00	***Cardiac***	
B01		***Anomalous pulmonary venous return***
B02		***Atrial Septal Defect***
B03		***Atrioventricular septal defect***
B04		***Cardiac septal defect***
B05		***Cardiac murmur NOS***
B06		***Congenital heart defect NOS***
B07		***Congenital pulmonary valve atresia***
B08		***Heart disease congenital***
B09		***Persistent fetal circulation (PDA)***
B10		***Tetralogy of Fallot***
B11		***Tricuspid valve incompetence***
B12		***Ventricular septal defect***
C00	***Congenital malformation NOS***	
C01		***Congenital anomaly NOS***
D00	***Chromosomal abnormality***	
D01		***Trisomy***
D02		***Partial trisomy 16 and partial monosomy***
E00	***Craniofacial/ENT***	
E01		***Accessory Auricle***
E02		***Ankyloglossia***
E03		***Anotia***
E04		***Branchial cyst***
E05		***Choanal atresia***
E06		***Cleft lip and palate***
E07		***Ear malformation***
E08		***Low set ears***
E09		***Mandibulofacial dysostosis***
E10		***Palpebral ptosis***
F00	***Gastrointestinal***	
F01		***Duodenal atresia***
F02		***Congenital megacolon***
F03		***Pyloric stenosis***
G00	***Hematological***	
G01		***G6PD deficiency***
G02		***Thalassaemia, alpha***
H00	***Orthopedic/musculoskeletal***	
H01		***Amniotic band***
H02		***Adactyly***
H03		***Chondrodystrophy***
H04		***Hip deformity***
H05		***Hip dysplasia***
H06		***Limb malformation NOS***
H07		***Polydactyly***
H08		***Talipes equinovarus***
I00	***Renal***	
I01		***Congenital hydronephrosis***
I02		***Kidney malformation***
I03		***Kidney duplex***
I04		***Renal aplasia***
J00	***Other specify:*** _____	

NOS=Not otherwise specified
PDA=Patent ductus arteriosus

K. Adverse events (AE) form

General instructions for the completion of non-serious adverse events form

If AE results in death, hospitalization, prolongation of existing inpatient hospitalization, or persistent or significant disability/incapacity, or if AE is immediately life-threatening, cancer, congenital anomaly/birth defect, due to overdose, or other important medical event, enter event on the serious adverse event (SAE) form.

Adverse events (AE)

	Field on the form	**Instructions**
1	Reporting date	Record the actual date of reporting the adverse event (dd/mm/yyyy)
2	Vaccination dose	Specify the link of the adverse event with the vaccination dose, e.g., if the adverse event occurs the day or within 15 days of the second dose, then it should be associated with the second dose, otherwise with another visit.
3	Any adverse event other than the current one	Indicate if the participant experienced any adverse event(s) other than the current one to previous doses of the same vaccine. If "yes" specify details.
4.1c	Adverse events	Whenever possible, provide a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, each symptom must be recorded on a separate line of the AE form. Please refer to the guidelines for side effect included on the back of this questionnaire.
4.2c	Type	Indicate the type of adverse events: - Systemic = any clinical AEs other than injection site AEs. - Injection site = occurs at the injection site only. - Other = neither systemic, nor injection site.
4.3c	Intensity	Indicate the intensity of adverse events: - Mild = Aware of symptom, but easily tolerated. - Moderate = Discomfort enough to cause interference with usual activities. - Severe = Incapacitating with inability to work or do usual activities. - Life-threatening = places the subject/patient at immediate risk of death from the experience as it occurred. - Death
4.4c	Possible cause	Indicate the possible cause or the relationship to HPV vaccine: - Definitely related = The adverse event and administration of vaccine dose are related in time, and a direct association can be demonstrated. - Probably related = The adverse event and administration of vaccine dose are reasonably related in time, and the adverse event is more likely explained by study agent than other causes. - Possibly related = The adverse event and administration of vaccine dose are reasonably related in time, and the adverse event can be explained equally well by causes other than study agent. - Probably not related = A potential relationship between vaccine dose and the adverse event could exist (i.e., the possibility cannot be excluded), but the adverse event is most likely explained by causes other than the vaccine dose. - Not related = The adverse event is clearly explained by another cause not related to the vaccine dose. Please refer to the guidelines for causality.
4.5c	Comment	If applicable, record as much information as possible to help complete adverse event data.

4.6c	Start reaction (date/time)	Date when the adverse event began. If laboratory or other AE enter the date of the laboratory exam or special safety exam.
4.7c	Stop reaction (date/time)	Record one of the following, as appropriate: - the date on which the participant no longer experienced the AE; or - the date of the study visit or specimen collection at the change in status/outcome is first noted.
5	Action taken	Indicate the action taken. Specify other action(s), if necessary.
6	Serious adverse events outcomes	If applicable, indicate serious adverse events outcomes. Specify other outcome(s). If not applicable, leave blank.
7	Remarks	If necessary, record as much information as to help complete adverse event understanding.
8	Staff Id	Indicate the Staff Id completing this questionnaire
9a	SAE reported to IARC	Record the actual reported date to International Agency for Research on Cancer (IARC) of serious adverse effect, if applicable. It should be reported within 24 hours of the site becoming aware if the SAE.
9b	SAE reported to LEC	Record the actual reported date to the local ethics committee (LEC) of serious adverse effect if applicable. It should be reported within 7 days.
9c	SAE reported to DCGI	IARC will notify DCGI and all the site PIs about unexpected serious adverse event within 14 days of its awareness and will notify the respective site the date of reporting the SAE to DCGI to be updated on this form.

1	Reporting date: *(dd/mm/yyyy)*	__/__/20__
2	Vaccination dose: *(1: first 2: second 3: third 4: other visit)*	☐
3	If 2nd or 3rd dose, did the patient experience any adverse event(s) other than the current one to previous doses of the same vaccine: *(1: no; 2: yes; 9: not known)*	☐
	If yes specify:	

4	*Adverse events (see below for code)*	*Type*	*Intensity*	*Possible cause*	*Comment*	*Start reaction (date and time)*	*Stop reaction (date and time)*
A	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h
B	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h
C	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h
D	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h
E	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h
F	☐☐☐	☐	☐	☐		__/__/20__ __:__h	__/__/20__ __:__h

Type: (1: systemic; 2: injection site; 3: other)
Intensity: (1: mild 2: moderate; 3: severe; 4: Life-threatening (serious); 5: death) Complete the SAE form if the response is 3, 4 or 5
Possible cause (due to vaccine): (1: definitely related; 2: probably related; 3: possibly related; 4: probably not related; 5: not related)

5	Action taken: *(1: reassured; 2: observation; 3: symptomatic treatment; 4: IP treatment; 5: rechallenge (further vaccination); 6: no further vaccination; 8: other (specify:))*	☐
6	Serious adverse events outcomes: *(1: fully recovered; 2: chronic sequelae (specify:); 3: death; 9: not known)*	☐
7	Remarks:	
8	Staff Id:	☐☐
9	If this is a SAE, specify dates if reporting it to IARC, local EC and DCGI:	

SAE reported to IARC:	Date: __/__/20__	○
SAE reported to local ethics committee:	Date: __/__/20__	○
SAE reported to DCGI:	Date: __/__/20__	○
Data entry done:		○

Guidelines for causality

Assessing the relationship of adverse experiences to test vaccine

The assessment of causality is reported according to the investigator's **best** clinical judgment. The confidence in a given classification increases as the number and/or intensity of its respective criteria increase.

CRITERIA	CLASSIFICATION
The participant did not receive the test vaccine. OR The temporal sequence of the AE onset **relative** to **administration** of the test vaccine is **not reasonable**. OR There is **another obvious** cause of the AE.	1 = **Definitely not** related to test vaccine
There is **evidence of exposure** to test vaccine. There is **another more likely** cause of the AE. Rechallenge (if performed) is **negative or ambiguous**.	2 = **Probably not** related to test vaccine
There is **evidence of exposure** to test vaccine. The temporal sequence of the AE onset **relative** to **administration** of the test vaccine is **reasonable**. The AE could have been due to **another equally likely cause**.	3 = **Possibly** related to test vaccine
There is **evidence of exposure** to test vaccine. The temporal sequence of the AE onset **relative** to **administration** of the test vaccine is **reasonable**. The AE is **more likely explained** by the test vaccine than by another cause.	4 = **Probably** related to test vaccine
There is **evidence of exposure** to test vaccine. The temporal sequence of the AE onset **relative** to **administration** of the test vaccine is **reasonable**. The AE is **more likely explained** by the test vaccine than by another cause. Rechallenge (if feasible) is **positive**. The AE shows a **pattern consistent** with **previous knowledge** of the test vaccine **or** test vaccine class.	5 = **Definitely** related to test vaccine

Guidelines for side effects:

MILD SIDE EFFECTS:

Do not generally affect the person's ability to carry on their normal activities and resolve quickly. Examples include:

A01	Abdominal cramps
A02	Acne
A03	Alopecia
A04	Back pain
A05	Bone pain
A06	Diarrhea
A07	Discomfort
A08	Dizziness
A09	Dry skin
A10	Fainting (vaso vagal reaction) within 15 to 20 m minutes of vaccine receipt
A11	Fatigue
A12	Injection site pain
A13	Joint stiffness
A15	Low-grade fever (<39°C sublingual
A16	Malaise
A17	Mild headaches
A18	Mild injection site swelling (≤ 2 cm)
A19	Mild irritability
A20	Mild muscle pain
A21	Mild pruritus
A22	Muscle cramps
A23	Muscle spasms
A24	Muscle tightness
A25	Musculoskeletal discomfort
A26	Nausea
A27	Neck pain
A28	Night sweats
A29	Pain in extremity
A30	Rash
A31	Redness, mild tenderness or bruising around
A32	Sensation of heaviness
A33	Shoulder pain
A34	Skin irritation
A35	Other specify: _____

MODERATE SIDE EFFECTS:

B01	Allergic reaction [Characterized by one or more of the following: (1) skin manifestations (e.g. hives, eczema); (2) wheezing; (3) facial or generalized oedema.]
B02	Allergic skin reactions
B03	Facial edema
B04	Generalized arthralgia
B05	Generalized edema
B06	High fevers sometimes associated with
B07	Larger reactions (> 2 cm) around the injection site
B08	Prolonged or excessive screaming/crying (< 3 hours) *[Inconsolable continuous crying lasting at least 3 hours accompanied by high-pitched screaming.]*
B09	Severe headaches
B10	Suppurative lymphadenitis
B11	Temporary joint pain or swelling
B12	Temporary lowering of the platelets (mild
B13	Other specify: _____

SEVERE:

C01	Anaphylactoid reaction (acute hypersensitivity reaction) [Exaggerated acute reaction, occurring within 2 hours after immunization, characterized by one or more of the following: (1) wheezing and shortness of breath due to bronchospasm; (2) laryngospasm/laryngeal oedema; (3) one or more skin manifestations, e.g. hives, facial oedema, or generalized oedema]
C02	Blood disorders
C03	Brachial neuritis
C04	Bronchial-asthma
C05	Cardiac disorders
C06	Episode of hypotonia and hyporeactivity
C07	Extreme fever (>40.5 °C)
C08	Eye disorders
C09	Gastro intestinal disorders
C10	Hemiplegia
C11	Immune system disorders
C12	Injection site abscess
C13	Kidney disorders
C14	Malignant neoplasm
C15	Nephritis
C16	Osteitis/Osteomyelitis
C17	Paraplegia
C18	Peripheral neuritis
C19	Pneumonia
C20	Psychiatric problem
C21	Seizures
C22	Sepsis
C23	Severe convulsions
C24	Severe local reaction (swelling beyond the nearest joint; pain, redness and swelling of more 3 days duration; requires hospitalization)
C25	Steven-Johnson syndrome
C26	Vascular disorders
C27	Other specify: _____

SERIOUS:

D01	Anaphylactic shock [Circulatory failure (e.g. alteration of the level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and/or laryngospasm/laryngeal oedema leading to respiratory distress occurring immediately after immunization.]
D02	Acute flaccid paralysis
D03	Bleeding disorders
D04	Cardiomyopathy
D05	Encephalitis
D06	Encephalopathy
D07	Guillain-Barré syndrome
D08	Meningitis
D09	Myocardial infarction
D10	Pulmonary embolism
D11	Septicemia
D12	Severe thrombocytopenia (less than 15,000
D13	Toxic-shock syndrome (TSS)
D14	Other specify: _____

L. Serious adverse events (SAE) form

Use this form if AE results in death, if AE is immediately life-threatening, results in persistent or significant disability/incapacity, results in hospitalization or prolongs an existing hospitalization, is a congenital anomaly/birth defect, a cancer, the result of an overdose or other important medical event.

- Inform IARC of serious adverse event, within 24 hours (as defined in Good Clinical Practices Guidelines).
- Inform Local ethics committee (LEC) of serious adverse effect within 7 days.
- IARC will notify Drug Controller General India (DCGI) about any unexpected SAE within 14 days.

Any unexpected serious adverse event (SAE) occurring during a clinical trial should be reported promptly (within 14 calendars days) by IARC to the licensing authority and to the other investigator(s) participating in the study.

This questionnaire is to be reviewed/completed at each visit.

Patient details

A	Field on the form	Instructions
1	Patient initials	Indicate the patient initials to keep the confidentiality.
2	Subject number	Indicate the subject number in the study. Use the 5 unique numbers used on the barcode to identify the patient anonymously (one letter + serial number 4 digits).
3	Gender	By default we will have only female.
4	Birthdate	Record the date of birth of the participant (dd/mm/yyyy).
5	Weight / Height	Indicate the participant's weight (in kg) and height (in cm).

Cervical Cancer Vaccination Programme (CCVP)
(RANDOMIZED TRIAL OF 2 VERSUS 3 DOSES OF HPV VACCINE IN INDIA)
Institute Name

SERIOUS ADVERSE EVENTS (SAE)

Barcode

A. Patient details

1	Patient initials: __/__ *First name / Last name*	2	*Subject number:*	
3	Gender: Female	4	Birthdate: *dd/mm/yyyy*	__/__/19__
5	Weight: ____ *(kg)* / Height: ____ *(cm)*			

Suspected drugs

B	Field on the form	Instructions
1	Generic name of the drug	By default the generic name will be: "GARDASIL - [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] - Merk and Co, INC"
2	Indication	By default the indication(s) for which suspect drug was prescribed is: "evaluate the comparative efficacy of 2- versus 3-dose regimens of HPV vaccination in preventing cervical cancer"
3	Strength	By default strength of the product is: Each 0.5 ml dose contains approximately 20 mcg of HPV6 L1 protein, 40 mcg of HPV11 L1 protein, 40 mcg of HPV16 L1 protein and 20 mcg of HPV18 L1 protein. Each 0.5 ml dose of vaccine contains approximately 225 mcg of aluminum (as amorphous aluminum hydroxyphosphate sulfate adjuvant), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, and water for injection.
4	Dose and regimen	By default the dose is 0.5 ml and the regimen is: 2 doses (Day 1 and day 60) or 3 doses (Day 1, 60 and 180). Mention if the participant is in the 2 or 3 dose arm.
5	Route of administration	By default the route of administration is always intramuscular.
6	Date 1st dose	Specify the date of the first vaccination according to the vaccination form.
7	Date 2nd dose	Specify the date of the second vaccination according to the vaccination form, if applicable.
8	Date 3rd dose	Specify the date of the third vaccination according to the vaccination form, if applicable.
9	Which dose	Specify after which dose of vaccine appears the SAE according to the list.

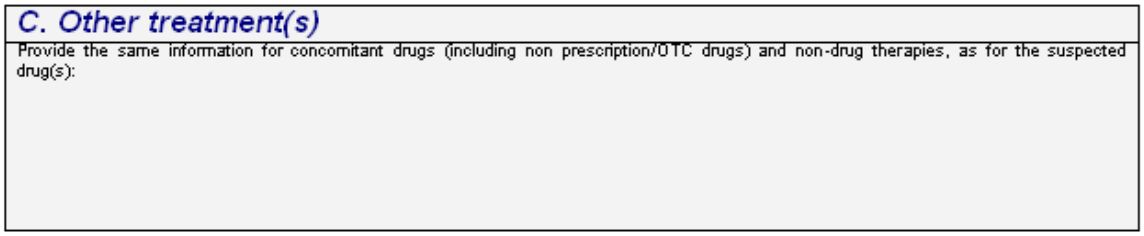
B. Suspected drug(s)

1	Generic name of the drug:	**GARDASIL - [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] - Merk and Co, INC**
2	Indication(s) for which suspect drug was tested:	**Evaluate the comparative efficacy of 2- versus 3-dose regimens of HPV vaccination in preventing cervical cancer**
3	Strength:	Each 0.5 ml dose contains approximately 20 mcg of HPV6 L1 protein, 40 mcg of HPV11 L1 protein, 40 mcg of HPV16 L1 protein and 20 mcg of HPV18 L1 protein. Each 0.5 ml dose of vaccine contains approximately 225 mcg of aluminum (as amorphous aluminum hydroxyphosphate sulfate adjuvant), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, and water for injection.
4	Dose and regimen:	*Dose:* 0.5 ml / *Regimen:* 2 doses (Day 1 and day 60) / 3 doses (Day 1, 60 and 180)
5	Route of administration:	Intramuscular
6	Date 1st dose of Gardasil*:	*Date:* __/__/20___ (dd/mm/yyyy)
7	Date 2nd dose of Gardasil*:	*Date:* __/__/20___ (dd/mm/yyyy) or not given
8	Date 3rd dose of Gardasil*:	*Date:* __/__/20___ (dd/mm/yyyy) or not given
9	SAE occurred after which dose of Gardasil*:	First / Second / Third

** Delete as appropriate*

Other treatment(s)

C	Field on the form	Instructions
1	Concomitant drugs information	Provide the same information for concomitant drugs (including non prescription/OTC drugs) and non-drug therapies, as for the suspected drug(s):



Details of suspected adverse drug reaction(s)

D	Field on the form	Instructions
1	description of reaction	Whenever possible, provide a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, each symptom must be recorded on a separate line of the AE form.
2	Start date (and time) of onset of reaction	Date when the adverse event began. If laboratory or other AE enter the date of the laboratory exam or special safety exam.
3	Stop date (and time) of duration of reaction	Record one of the following, as appropriate: - the date on which the participant no longer experienced the AE; or - the date of the study visit or specimen collection at the change in status/outcome is first noted.
4	Dechallenge information	Record information about dechallenge *- Definition: withdrawal of a product from the patient's therapeutic regimen.* *- Negative dechallenge: continued presence of an adverse experience after withdrawal of the drug.* *- Positive dechallenge: partial or complete disappearance of an adverse event after withdrawal of the product.*
5	Rechallenge information	Record information about rechallenge *- Definition: reintroduction of a product suspected of having caused an adverse event following a positive dechallenge.* *- Negative rechallenge: failure of the product, when reintroduced, to produce signs or symptoms similar to those observed when the product was previously introduced.* *- Positive rechallenge: reoccurrence of similar signs and symptoms upon reintroduction of product.*
6	Setting	Specify the setting (e.g. hospital, out-patient clinic, home, nursing home)

D. Details of suspected adverse drug reaction(s)		
1	Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction:	
2	Start date (and time) of onset of reaction:	*Date:* __/__/20___ *(dd/mm/yyyy) / Time:* __/__ h
3	Stop date (and time) of duration of reaction:	*Date:* __/__/20___ *(dd/mm/yyyy) / Time:* __/__ h
4	De-challenge information:	NOT APPLICABLE
5	Re-challenge information:	
6	Setting: *(hospital, outpatient clinic, home)*	

Outcome

E	Field on the form	Instructions
1	Recovery/any sequelae	Specify Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted
2	Cause of death	Specify a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings
3	Other information	Specify other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

E. Outcome	
1	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted:
2	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-morten findings:
3	Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

Details about the investigator

F	Field on the form	Instructions
1	Name of investigator	Specify the name of the investigator
2	Address of investigator	Specify the address of the investigator
3	Telephone of investigator	Specify the phone number of the investigator
4	Profession	Specify the profession and specialty of the investigator
5	Signature	Add the signature of the investigator

F. Details about the investigator		
1	Name:	
2	Address:	
3	Telephone number:	
4	Profession:	*(speciality)*
5	Signature:	

Reporting information

G	Field on the form	Instructions
1	SAE reported to IARC	Record the actual reported date to International Agency for Research on Cancer (IARC) of serious adverse effect, if applicable. It should be reported within 24 hours of the site becoming aware if the SAE.
2	SAE reported to LEC	Record the actual reported date to the local ethics committee (LEC) of serious adverse effect if applicable. It should be reported within 7 days.
3	SAE reported to DCGI	IARC will notify DCGI and all the site PIs about unexpected serious adverse event within 14 days of its awareness and will notify the respective site the date of reporting the SAE to DCGI to be updated on this form.

Data entry done:		○
SAE reported to IARC:	Date: __/__/20__	○
SAE reported to local ethics committee:	Date: __/__/20__	○
SAE reported to licensing authority (DCGI)	Date: __/__/20__	○

Definitions:

- *Positive dechallenge reactions: an adverse event which disappears on withdrawal of the medication*
- *Negative dechallenge reactions: an adverse event which continues after withdrawal*
- *Positive rechallenge reactions: symptoms re-occuring on re-administration*
- *Negative rechallenge reactions: failure of a symptom to re-occur after re-adminstration*