**Title**

**Audio-video informed consent process in vaccine trials: Experience from North India**

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**Abstract**

The audio-video (AV) recording of the informed consent process of each participant in a clinical or vaccine trial has become one of the essential requirement to obtain prior ethical approval from the institute’s ethics committee and Drug Controller General of India to conduct such trial. This ensures the voluntary participation of each participant. This paper describes the experience of the authors with the audio-video consenting process during a phase III rotavirus vaccine trial among healthy infants in Chandigarh, North India. Among 105 subjects who expressed their initial willingness to be a part of the trial, all agreed to undergo AV informed consenting process, out of which 100 (95.2%) were finally consented to participate, and were enrolled in the study. AV recordings of 100 patients were transcribed, and later translated in English language to perform the thematic analysis of the text. A total of 105 queries were raised by 55 participants. Majority of the queries were around where to consult in case of any emergency (22/105, 21%), risks to the baby as a result of the vaccine (20/105, 19%), vaccination schedule and any change in it (15/105, 14%), and had to go out of the city (10/75, 9.5%). All the queries were patiently listened and responded, which allayed most of their fears especially, related to adverse effects of the intervention. AV consenting process ensured transparency and accountability of the investigators, responsive referral mechanism in case of adverse events, building an initial rapport with the participant, complete vaccination of the trial subject (infant) and providing free option for private care consultation depending upon the willingness of the parents. These strengths of the audio video consenting might have led to higher participation rates of the subjects in the trial in this study.

**Introduction**

In the last decade, serious concerns have been raised regarding the lack of adherence to ethical conduct during recruitment of vulnerable subjects in clinical trials in India (1). Although it is mandatory under Schedule Y of the Drugs and Cosmetics Rules 1945 to obtain a freely given informed, written consent from study subject before enrolment in a clinical trial, there have been several complaints about the misuse of this provision by research institutes, pharma companies and Clinical Research Organizations who are engaged in clinical trials (2). It was reported that many a time the informed consent was taken from the participating subjects without informing them about the benefits and, especially, the harmful side effects of the investigational product in the trial (3). It is assumed that subject will not be able to understand too much technicalities involved in the trial, hence only the most essential information being provided to the subject and informed consent used to be taken (3).

Taking a serious note of that, the Office of the Drug Controller General of India (DCGI) with the approval from Ministry of Health and Family Welfare has made audio-visual recording of the informed consent process of each trial participant essential in addition to the written informed consent (4). The AV recording and related documentation should be preserved safely, confidentially and secured in password protected software after the completion / termination of the study for at least a period of 5 years if it is not possible to maintain the same permanently. These directives by the DCGI has not only made the pharmaceutical companies more wary of the situation but also cautioned the investigators who will be involved in conducting the trials, which may influence their decision in participating/conducting such trials.

Earlier studies have shown that more than one-third of the study subjects ranging from 30-50% refused to give consent for A-V recording of consent process. Not interested in recording or don’t like to be recorded, discomfort with and suspicion of being videotaped, feeling shy and hesitancy were the common reasons for refusal by the study subjects (5-8).

This paper describes the experience of the authors obtaining audio-video consent from subjects’ (healthy infants) parents in phase III rota vaccine trial, so as to document the process involved in audio-video consenting. These findings will be useful for investigators/researchers in following the audio-video consenting process while conducting trials, and may allay their apprehension regarding increase in refusal rate by the participants.

**Methods**

Audio video (AV) consenting was done to take consent from the parents/guardians/legally accepted representatives (LAR) of healthy infants of age 6 to 8 weeks in a phase III rotavirus vaccine multicentric trial in India [9]. This trial was sponsored by Shantha Biotech Limited (A part of Sanofi Company). In this paper we are sharing the experience of AV consenting at one of the site at Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh. AV informed consenting process was used for recruiting 100 healthy infants into this trial in accordance with the new rules laid down by the DCGI at this site. The Institute Ethics Committee of PGIMER had approved the main trial.

**Setting of audio-video consenting**

A portion of a room was dedicated for AV process through artificial barriers to maintain confidentiality and to cut-off outside noise for better clarity of audio recording. Recording was done using a webcam (Logitech HD Webcam) mounted on a desktop. The investigators were trained to carry out the AV recording by showing dummy video on how to obtain audio video consent by the experts from the sponsors. At the first step consent to record audio and video of consent was obtained from the parents/guardians/LAR. Only if they agree then the AV informed consent was obtained.

The content of informed consent form is given in Box 1. The written informed consent form was in English, Hindi and Punjabi Languages. A structured AV consent module was followed to ensure that all the components of the informed consent were covered. All the contents were given equal importance while explaining to the prospective subjects. Adequate time was given for the discussion and settling the queries. Information was given in most understandable language. In case of illiterate subjects AV consenting was done in the presence of impartial witness. Consent form was signed by the parents/guardians/LAR under AV recording and a copy of ICF was given to the participant for records. Study investigators were trained for the AV consenting process and they remained throughout the trial.

**Data source and analysis**

Data were extracted from the archived trial database. Audio-video recordings were first transcribed in local language and then translated in English. Since this was qualitative data, hence, thematic analysis of the translated text was done manually by the study investigators (MG and JPT). Documentation of the process of AV consent, queries raised by the participants and responses by the investigator was also done. Socio-demographic characteristics of the participants were summarized using percentages.

**Results**

Table 1, describes the content of the AV informed content process along with its detailed description. Out of 155 subjects (infants accompanied by parents) who were contacted to be a part of the study, 105 expressed initial willingness to be a part of the study. Among those 105 subjects, all of them agreed to undergo AV informed consent, out of which 100 (95.2%) were finally enrolled into the study. Of them, more than half (58%) of the infants were males, three-fourth (76%) coming from rural areas with annual household income ranging from INR 12,000 - 4, 80, 000. The infant was accompanied by father and mother in 65% of cases and only mother in 31% of them, majority of them were housewives (57%). Nearly 62% of the parents who accompanied the subject were educated upto matriculation.

Out of 100, 55 (55%) subjects’ parents had asked any query. A total of 105 queries were raised with 27 (27%) asking only one query each, 12 (12%) asking two queries, another 12 (12%) had three queries, two (02%) had four queries and two (02%) of them even asked five queries each. Majority of the queries were around where to consult in case of any emergency (22/105, 21%), risks to the baby as a result of the vaccine (20/105, 19%), vaccination schedule and any change in the schedule (15/105, 14%), and what if I had to go out of the city (10/75, 9.5%). Some of them also had questions on the financial implications of enrolling into the study and whether they can avail private hospital care as well about the study procedures and what are the results of the trial till yet. Table 2 describes some of the queries raised by the subjects’ parents and the point wise reply given by the author during the AV informed consenting process. All the participants were informed about study procedures of the trial including number of visits required, when follow up was required, related adverse events etc., and given free chance to agree or disagree to participate in this study.

**Discussion**

The study demonstrated high participation rates of the subjects in the trial after audio video consenting. Below, we discuss the strengths of this process, as observed in the study, which might explain this phenomenon. Despite fears and apprehensions about the AV consenting process, all the subjects in a vaccine trial who expressed initial willingness to be a part of the study agreed to undergo AV informed consent without any refusals although they belonged to different cultural groups, gender, socio-economic status, education levels and occupation. Explaining the process and purpose of AV consent and addressing the queries seemed to instil confidence among subjects in the conduct of the trial. AV consent process takes a considerable amount of time, but it is a one-time activity and deserves the time it warrants.It has been reported in other studies that AV recording of clinical trial consenting increases the transparency of the informed consent process, which is similar to the findings of this study as all the participants were told about every aspect of the trial and given free chance to raise queries related to the trial and to agree/disagree to give consent to participate (1). This reassures the regulatory authority about the practice of clinical trial standards and ethics and re-establishes society’s faith in clinical research. AV recording not just protects the rights, safety and well-being of the subjects enrolled in the trial, it will actually play a key role in safeguarding the interests of all stakeholders in the clinical trials (1). In case of any dispute/litigation the investigator will be able to demonstrate hard evidence that all relevant information was provided to the potential participant before he/she understood and voluntarily agreed to take part in the clinical study. Introduction of the AV recording could also improve the conduct of the informed consent process because the process is recorded. A systematic review by Synnot et al (2014), reported that AV consent improves participant satisfaction with the consent information provided (12). It also implies that conduct is given more importance over mere documentation of the whole process. This ensures that incidents like the one which reported irregularities in the conduct of study and informed consent in a Human Papilloma Virus (HPV) vaccine trial does not happen again (10-11).

Not surprisingly, most of the queries reported in this trial during AV consenting were related to the apprehensions about the risks to the subject as a result of the vaccine. The minor side effects were already known to most of them, but the major risk i.e. intussusception in case of rotavirus vaccine in this study was a cause of concern for most parents. However, the authors felt that discussion with the anxious parents allayed most of their fears. It also helped build a healthy rapport between the parents and the investigator.

Parents were apprehensive about where to consult in case of any emergency. The trial had clearly written standard operating procedure for referral and management in case of any emergency in collaboration with the Department of Pediatrics and Radiodiagnosis at nearby tertiary care health facilities, which were around 4-6 kilometres from the study area. This was told to each participant during AV consenting. The mobile number of the project field staff was shared with the participants who used to facilitate the process. The parents also were given the option of consulting any private physician if needed. In the event of any private consultation, they were reimbursed if they incurred any expenditure.

Another fact that might have led to better participation rates is that the study investigators belong to a reputed medical institute in the region and have been providing medical care in the region since many years as part of a community outreach programme. They have also been involved in door-to-door primary health service delivery through a team of field workers. This might have facilitated the initial trust building.

There were quite a few questions on the existing vaccination schedule of the infant and any change in it as a result of this vaccine. As the trial was being conducted adjacent to the Maternal and Child Health Centre, the infant was linked to the nearby immunization centre. The project staff ensured complete vaccination of the child as per the schedule and facilitated the process in every visit which also helped in building a personal rapport. After the administration of the trial vaccine, the subject was linked to the nearby vaccination centre for subsequent vaccinations which also assured the parents.

Challenges of AV recording of informed consent process in clinical trials include the need for a dedicated room for recording and equipment which has significant cost implications, training of personnel, time consuming process, reluctance of participants to undergo recording and issues of data storage and safety. In this age of technology where almost everyone has a gadget with a video recording facility and sharing videos and photos has become so routine in our daily lives, reluctance to undergo video recording is a myth now. However, in India, due to the cultural barriers females especially in rural India are not comfortable being videotaped and that too in front of a male investigator.

**Conclusions**

The study showed high participation rates in a vaccine trial with AV consenting process. The descriptive and rigorous process of audio video consenting helped in building trust of the participants on the investigators, allayed their fear and apprehensions, which might have increased the participation in this study. However, it is suggested to formulate more clear guidelines or standard operating procedure to standardise the process of AV consent, like to have list of frequently asked questions with the answers, and also related to the specification of the device to be used for recording.

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**Table 1. Content of the Audio-Visual informed consent process**

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| --- | --- |
| **Content** | **Description** |
| Introduction | Introduction of self and the participant; welcoming the participant into the trial; inviting queries; build rapport |
| Thanking the participant for agreeing to the AV recording | Build rapport; make the participant comfortable |
| Background and rationale of the study | Rotavirus infection among infants and children; severity; incidence; symptoms; role of rotavirus vaccine |
| Number of children participating in the study | Total sample size; sample to be recruited from each centre in a multi-centric trial |
| Purpose of the study | Evaluate the ability of the new rotavirus vaccine under trial to produce antibodies which may have the ability to prevent infection from rotavirus compared to an approved vaccine |
| Length of participation | Participation will last for 12-15 weeks upon completion of 28 days post third dose |
| Study procedures | No undue influence to participate; ample opportunity to enquire about the details the study; signing the ICF; evaluation of the child as per the inclusion and exclusion criteria; recruitment into the trial |
| Description of the intervention | Details of the vaccines to be administered; blood sampling; stool sampling; home visits; diary cards for monitoring of adverse reactions and other health events; |
| Study visits | Timing of visits; activities during each visit; home visits |
| Risks and side effects of participation | Minor and major side effects of each vaccine; intussusception; referral mechanism in case of any adverse reaction |
| Payment for taking part in the study | No payment except travel expense incurred to reach the site; free vaccines; health care costs on the chid during the study period will be borne |
| Possible benefits for taking part in the study | No direct benefit; benefit of health examination and general health discussions with the study doctor; |
| Possible benefits to others | Benefit to the community |
| Other available treatments | You can choose to purchase available vaccines against rotavirus from the market |
| Voluntary nature of participation | Voluntary participation; no undue influence |
| Compensation and treatment |  |
| Responsibilities of the participant | Follow the instructions; return to the clinic for scheduled visits; complete the diary card; promptly report to the staff of any unexpected or serious health events; inform the study doctor of any medications your child take during the study |
| Termination of participation | Do not follow the instructions; sponsors or regulatory bodies decided to stop the study |
| Confidentiality | Child’s participation will be kept confidential; auditors, ethics committee, regulatory authorities will be granted access to your medical records |
| Right to refuse or withdraw | You may choose to stop your child’s participation in the study at any time you wish |
| Dissemination of new information | You will be informed of any new things about the vaccine |

**Table 2. Queries by the participant and reply by the author during the AV informed consent process**

|  |  |  |
| --- | --- | --- |
| **Contents of the AV consent module** | **Queries by the participant** | **Reply/comments of the author/s** |
| Introduction of self and the participant | *None* | Author’s observation: It helped in developing a rapport between the investigator and the subjects’ parents/guardian |
| Thanking the participant for agreeing to the AV recording | *None* | Author’s observation: A wonderful gesture which further strengthened the rapport |
| Background and rationale of the study | *None* | None |
| Study procedures | *“Kya hum bahar se bhi yeh tika laga sakte hain?”( Can we get this vaccine from outside)* | Author’s reply: This particular vaccine is not available in the market. However, there are two other varieties of rotavirus vaccines available in the market manufactured by different companies. But it is not available in government facilities, you have to purchase it from outside. |
| Length of participation | As the length of participation was 12-15 weeks long, many participants had some other plans during this period.  *“Hume to gaon jana hai, kya hum tike gaon mein laga sakte hain” (We have to go to our native place, can we get the vaccine there)* | Author’s reply: You can go to your village for a week or so but you have to inform us well before you plan for the trip. However, in case you plan a long trip of 1 month or more, we are afraid we cannot enrol the subject in this study. If you are still interested to participate in this study it is better if you consult with your family members regarding your travel plans in the next 3 months and let us know. |
| Description of the intervention | *“Diary card bharna kya jaruri hai, kaise bharna hai” (Is it necessary to fill the diary card, how to fill it?)* | Author’s reply: Diary card helps us to keep a record of the daily health events after vaccination so that any adverse reaction can be picked up early for immediate action. Diary card is very easy to fill (diary card shown to them) with simple questions about the health of your child in local language. You just have to circle the correct response. (demonstration done) In case of any difficulty in filling the card, please feel free to contact us. |
| Risks and side effects of participation | Parents were found anxious over the side effects of the vaccine.  *“Bachhe ko koi dikkat to nahin hogi”“Agar bachhe ko koi dikkat ho to hum kya kare”(Will there be any difficulty to the child, in that case what should we do?)*  *“Agar raat ko bachhe ko koi dikkat ho to kya kare” (If the child has any difficulty at night, what should we do?)*  *“Humein intussusception ke bare mein kaise pata chale”(How do we know about intussusception?)*  *“Kitne bachhon ko intussusception hota hai”(How many children suffer from intussusception?)*  *“Abhi tak jitney bachhon ko apne yeh vaccine pilayi hai, kisi ko aisi dikkat aayi hai” (Among the children whom you have vaccinated till now, has anyone suffered from this kind of problem?)* | Author’s reply: Vaccines are not without any side effects. There are some minor and some major side effects. However the risk of major side effects like intussusception is very rare. We have to weigh the benefits and risks of administering a vaccine. Moreover, rota virus vaccines available in the market also have similar risk of side effects. In case of any difficulty, please feel free to contact our project staff at the numbers mentioned in the form at any time of day. Come immediately to this facility and consult the specialist at room no-3. In this project we also have paediatricians from premier tertiary care institutes as co-investigators. In case of a serious event, we will facilitate your visit to a paediatrician in either of the facilities. We have a referral mechanism in place for any untoward event.  Author’s reply: In case of inconsolable cry, blood in stools, fever or vomiting, immediately contact our project staff.  Author’s reply: There is very small risk of intussusception, around 1 in 100000 infants. However, this risk is also present in other licensed rotavirus vaccines available in the market.  Author’s reply: Till now, no reports of any serious adverse event related to the vaccine such as intussusception has come to notice in this project. |
| Study visits and vaccination schedule | *“Agar hum tike lagana bhul jaye to...” (If we forget to vaccinate the child, then…)*  *“kya aap sare injection yahan lagaoge” (Will you give all the vaccinations here)*  *“Kya hum BCG vaccination laga sakte hain” (Can we administer BCG vaccination)*  *“agar aap yahan tike lagaoge toh humein kahin aur lagane ke liye jaana padega kya?”*  *(if I get my child vaccinated here, do I need to take him to some other place for other vaccinations)* | Author’s reply: Don’t worry. We will remind you about the vaccination date of your baby in advance and also on the day of vaccination through phone calls.  Author’s reply: Yes, you will get full vaccination schedule here for the first three months, after that we will link you to the nearby government dispensary where you will get all the subsequent vaccinations  Author’s reply: Yes, you can administer BCG to the child, there is no problem.  Author’s reply: You will get full vaccination schedule here for the first three months, following which we will link you to the nearby government dispensary where you will get all the subsequent vaccinations. |
| Responsibilities of the participant and termination of participation | *“Hum to bachhe ko sare tike lagwana chahte hain, lekin agar koi problem hui toh?” (We want to vaccinate our child completely, but in case some difficulties arise, then?)* | Author’s reply: In case of any difficulties, don’t hesitate to contact us, we will help you. |
| Other queries | *“Kya hum private hospital main dikha sakte hain” (Can we consult a private hospital)*  *“Kya bahar ki dawai ke paise milenge” (Will you reimburse the money spent on medicines bought outside)* | Author’s reply: Yes, you can consult any doctor whose qualification is at least MBBS  Author’s reply: Yes, we will reimburse you the money you spent on medicines purchased from outside, but we would need a bill of that for our records |