Review Article

Exemption from informed consent: When it is possible in investigational product and drug trials?

ABSTRACT

One of the most important ethical step in conducting investigational product trials or drug trials is obtaining informed consent from the participants. Although consent from the participants regarding participation is of prime importance but is not always practical or feasible. There may be several instances where it is practically impossible to obtain informed consent, whereas in some cases, obtaining informed consent from the trial participants adversely affects the quality and validity of the study data. Obtaining informed consent is a highly complex and technical process if the participants are not literate or suffering from a terminal illness, Also in some instances obtaining informed consent regarding the washout of prior prescribed medicine which may affect the trial outcomes. Although many guidelines exist for obtaining proper informed consent while very scarce literature exists on the instances where it can be waived off. Therefore, this brief narrative review aims to provide insight into currently available knowledge about when to obtain informed consent during testing of investigational product trials and drug trials and other possible scenarios where it can be waived off considering the effects of the washout period.

Key words: Cross-over studies; humans; informed consent; medicine; prescription drugs; washout period

Introduction

Several biomedical researches are conducted around the globe to improve health outcomes prolonged human life. These researches or trials involving humans allocate the participants to one or more groups so to test the single or many health-related interventions. These trials may range from testing of drugs, cosmetics products, and medical devices to even testing a newly developed surgical procedure.[1] But before any research or investigational intervention, it is the ethical and moral duty of the researcher to obtain informed consent from the participants.[2]

Informed consent is a procedure in which the researcher or the physician conducting the research, gives a transparent explanation to the participants of all the risks, benefits, and alternatives of a given procedure or intervention before the research. This procedure not only educates the participants but also makes them competent to decide voluntarily about whether they want to be a part of the ongoing interventional research/procedure or not.[3,4]

There are instances where a research involves single blinding of the participants and they receive a placebo in place of an investigational product or a drug, and in some instances,

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cases and trials are conducted in a cross-over design manner requiring a long washout period of prescription medication which the participants are taking for a long time regarding their medical conditions.[5-7]

In simple terms, a washout period is a time duration during a research or trial, when the study subject/participant is taken off an interventional drug or other prescribed medication to minimize or eliminate the effects of the drug.[8]

Withholding or stopping of the prescription medication (washout period) is the most widely used method in drug research trials. Generally, these washout periods are justified when informed consent is ethically obtained from the subjects being participating in the study and there is no harm to participants for temporary halting such prescribed medications, also it is essential for both patient safety and scientific reliability. But on the contrary, when the participants are single-blinded by the means of placebo or a long-duration washout period, obtaining informed consent becomes of prime importance. Although these single-blinded studies are less widespread but still common.[9,10]

Hence, the procedure of obtaining informed consent in such mentioned trials is well understood, where it is possible and practical to be obtained before the study, still there is dilemma about the cases where it can be waived off. Thus, this brief narrative review aims to provide an insight into currently available literature about the actual time for obtaining informed consent during testing of investigational product and drug trials, and other possible scenarios where it can be waived off.

The situations in which it is extremely important to take informed consent for washout of the prescription medication before the subject is treated with investigational product or drug are:[11,12]

- When the subject being recruited in the study does not suffer from a life-threatening condition and can provide informed consent.
- When the subject is suffering from a life-threatening condition with sufficient time, also other legal representatives are which are available to provide the consent.
- When there is already existing medication which is equally beneficial for the participant for improving the outcome, and the trial is being conducted for equipoise and require washout period of prescribed medicine thus imposing them to additional threat of adverse outcomes.
- When the participants are aware that the investigational product may be very different from the standard medicines which they currently are aware of.
- When the washout period for prescription medicine is sufficiently long and may increase the risk of known adverse events.

There is some exception of informed consent for the washout period of prescription medications:

It is moral duty and rule for every researcher that informed consent is taken before involving any patient in the study and this even holds when a participant is subjected to a washout or no-medication period of prior medication. However, there are certain scenarios where this process of informed consent can be exceptions which are as follows.

Impossibility of informed consent during emergency research:[13,14]

These are the researches where there is a life-threatening situation to the patient's life and require immediate medical intervention of care to protect him/her from potential harm. In this scenario, informed consent can be exempted as any time spend in disclosing the information and obtaining the informed consent can result in adverse outcomes concerning patient life.[13,14]

So, there is a limited period and also applicable to certain researches only where these informed consents can be exempted and require human subjects who are suffering from life-threatening condition and need prompt medical intervention but could not give informed consent because of their medical conditions, or when there is no means of alternative methods of obtaining consent, or in a case when they do not have a legally acceptable representative.

Detailed guidelines has been released by the USA's Food and Drug Administration on such emergency research where consent can be exempted:[13,14]

- When the study subjects are suffering from life-threatening conditions and require urgent intervention or care.
- Already existing treatments are not satisfactory or are not proven to provide benefits.
- Before conduct such emergency research in which informed consent is exempted, extensive research on the safety and effectiveness of the intervention should have already been carried out.
- It should have been otherwise impossible to take informed consent of the study participant because of his/her medical conditions.
- Intervention being delivered should have direct benefit to the subjects with regards to their life-threatening condition.
- The research could not practicably be carried out without exempting the informed consent.

When there is a threat of undermining the data quality and validity:

In drug trials, the quality or validity of outcome data is of prime importance. These data in many instances are purely based on self-reporting. So, in such cases when taking informed consent from a participant grading washout period of prescription may influence or highly compromise the inclusion rate of the participants and thus undermining the quality and validity of the data, the researchers can be exempted from obtaining the informed consent.[13,14]

Situation creating confusion or distress among participants:

Another circumstance that can lead to exemption of informed consent is the situation where obtaining informed consent may impose the participants to unnecessary distress or confusion.

For example, patients with life-threatening diseases who are purely focused on their treatment and speedy recovery and imparting additional information about the no-medicine period (washout period) will impose them to more distress and confusion and thus may influence the outcome.[13,14]

Certain community-based drug intervention:

Situation in which the research or the drug trial was designed by considering the views and involving representatives of the community from which the subjects are recruited. In such scenarios where such considerations had already been done by the institutional review board for approving the study, the researchers may apply for a consent waiver for the essential washout period of prescribed medicines.[13,14]

Other criteria for exemption of informed consent in prescribed medicines:

Other necessary things which are to consider for allowing waiver of informed consent regarding washout period of prescribed medicine should be of short duration and should not impose the subjects to risk no more than minimal risk and such wavier off should not alter or adversely affect the rights and welfare of the subjects.[13,14]

Conclusion

Various investigational product trials or drug trials, with variable washout periods for the prescription medications used by the subjects, are conducted around the world to improve the health outcomes. These trials on one hand provide opportunities to develop and test newer products or drugs, whereas on the other hand impose challenges and issues in conducting them specially at the time of obtaining informed consent. Still very little is known regarding when these informed consents can be waived off and still lots of confusion and uncertainty prevails. Hence, it is extremely important that Institutional Review Boards (IRBs) along with researchers and legally available representatives of the subjects come together and determine the most appropriate and easy method for obtaining informed consent in such difficult instances, and when to provide a waiver. All of which should be determined based on the type of medical condition the subject suffering from, the ability to give informed consent, type of study design, and minimal risk imposed by such washout periods. From this brief narrative review, the author hopes to throw some light on this regard and wish to attract the attention of various stakeholders toward this area.

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Conflicts of interest

There are no conflicts of interest.

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