

PAYMENT OF TRIAL PARTICIPANTS IN SOUTH AFRICA:

ETHICAL CONSIDERATIONS

FOR RESEARCH ETHICS COMMITTEES

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1. PURPOSE

The purpose of this document is to propose to Research Ethics Committees (RECs) certain considerations for payment of clinical trial participants in South Africa.

2. BACKGROUND

There has been controversy in South Africa and other countries as to whether trial participants should be paid and if so, for what and how much. On the one hand, there are concerns that even modest payments may cause participants to enrol in trials without duly considering the risks, thereby acting as an undue incentive and exploiting the situation of vulnerable participants. On the other hand, concerns have been raised that participants deserve appropriate compensation for their contribution to clinical trials.

This area of research ethics is a complex, controversial one where even reasonable people may not always agree. People may intuitively (or explicitly) favour a particular model of payment. For example, people who advocate that participants should be paid for expenses only are favouring a Reimbursement model. People who advocate that participants should be paid for their contribution in terms of time and burden-assumption are favouring a Compensation model.

In South Africa, at present, clinical trial participants tend to be paid R150 per visit. The Medicines Control Council (MCC) has recommended that trial participants be reimbursed a *minimum* of R150 per trial visit. This recommendation was made at the time that the National Health Research Ethics Council was not formally constituted. While not necessarily intended as a "flat rate", this approach may have been understood and applied as such by stakeholders.

3. CURRENT APPROACHES TO TRIAL PAYMENT: PROS AND CONS

The MCC recommendation has apparent advantages in that it is relatively easy to administer, and it appears fair because most trial participants across the country tend to get paid a similar basic amount unless there are additional specific and justifiable costs.

However this approach has a number of disadvantages that may lead to unfairness and inequity:

- Most trial participants are paid a similar amount, even when they may be assuming very different **research burdens** (time and inconvenience). For example, Participant A in a vitamin trial who spends 1 hour at a site and fills in a simple questionnaire may be paid R150, while Participant B in a microbicide trial who may spend 3 hours at a site, and undergoes counselling, HIV testing, examinations like colposcopy and social harm monitoring is also paid R150.
- Furthermore, trial participants are paid a similar amount, even when their actual **expenses** may be very different. For example, Participant C who spends R50 on travel, R20 on food and R100 on child-care (i.e. R170,00) will not be fully reimbursed for their expenses, whereas Participant D who spends R10 on taxi-fare has “made money” from the arrangement.

In both cases, the payment of a flat rate may allow unfairness to arise. Additionally, this approach to payment may act as an inappropriate incentive that undermines the autonomous decisions of trial participants to enrol in research. That is, it is possible that participants may minimise their concerns about the risks or pay inadequate attention to the risks in order to access the payments. This is particularly the case where participants are drawn from vulnerable groups, where conditions already exist that may compromise their ability to give authentic informed consent. This is also the case where payment exceeds *actual* research burdens (time, inconvenience) or direct expenses.

The possibility of “undue inducement” can be reduced by good consent procedures that help participants to process risks and by quality ethical review to minimize research risks. In addition, sound screening processes can offset the possibility that participants conceal information in order to access trial payments. Because both informed consent and ethical review are imperfect processes, where efforts can be made to improve payment approaches directly, these should be undertaken.

Lastly, this approach may undermine the role of RECs who are properly placed to make decisions about the appropriateness of payment amounts and schedules in the context of a full assessment of the risks and benefits of the trial, and information provided by the investigators about the study.

4. CONSIDERATIONS FOR PAYMENT OF TRIAL PARTICIPANTS

For the reasons cited above, this document proposes that RECs should take account of the considerations listed below when deciding about payment in trials. Such decisions should be specific to the trial at hand, defensible in terms of ethical principles and balanced in their protections of trial participants whilst facilitating the conduct of meaningful research.

RECs may wish to ask investigators to propose payment in accordance with these considerations.

The amount and schedule of payment to participants should depend on the following three components:

- 4.1. Trial participants should be compensated appropriately for their time.**
- 4.1.1. It has been recommended by some commentators that time payments should be made at rates commensurate with unskilled labour rates. This acknowledges that trial participation (while valuable) does not necessarily require special skills and training, but does entail expending effort. For example, hourly rates for unskilled civil engineering workers are approximately R10.00 per hour in South Africa.
 - 4.1.2. The above recommendation recognises that payment is being made for what the 'work' of research participation is worth, and not what the participants' actual time is worth.
 - 4.1.3. Even if participants are not formally employed, it could be considered that participation in research may compete with efforts to find other similar economic opportunities and that participants forgo other opportunities while they are engaged in trials, therefore participants should be compensated for their time.
 - 4.1.4. *Investigators could be asked to estimate the amount of time participants will spend engaged in research activities for each trial visit.*
- 4.2. Trial participants may be compensated for inconvenience.**
- 4.2.1. In some studies, participants will be required to undergo certain procedures that may cause inconvenience or discomfort. Consideration should be given to compensating participants for this inconvenience, over and above time payments.
 - 4.2.2. Payment amounts for inconvenient procedures should reasonably reflect the extent of such inconvenience. For example: the inconvenience attached to answering a simple and unobtrusive questionnaire may be lower than a blood draw.
 - 4.2.3. Slightly higher payments for inconvenience may complement time payments that usually turn out to be very modest.
 - 4.2.4. *Investigators could be asked to judge whether participants will undergo certain inconvenient or uncomfortable procedures at select trial visits.*
 - 4.2.5. Over time additional payments for particular inconvenient procedures could be standardized.
 - 4.2.6. It may be beneficial for RECs to communicate with each other regarding their compensation rates for inconvenient procedures that they consider acceptable.
- 4.3. Trial participants should be reimbursed for their expenses.**
- 4.3.1. Direct costs incurred by participants for research participation should be reimbursed.
 - 4.3.2. *Investigators could be asked to estimate costs that participants will incur because of their research participation.*
 - 4.3.3. The costs of participation could be established in consultation with community representatives who may be familiar with expenses for, for example, travel, parking, meals or child-care. Investigators are well-placed to consult representatives regarding these expenses.
 - 4.3.4. RECs could prospectively approve lower and upper limits of expense payments, which will have to be tailored somewhat to participants' actual expenses.
 - 4.3.5. The cost for participants of being away from their individual place of work should not be considered (see 4.1.2. above).

Consideration of the above elements is likely to ensure carefully justified payment amounts and schedules. After such careful consideration, it may not be necessary or appropriate to provide adult participants with such payments 'in-kind'.

In addition, completion bonuses would not be supported on this particular model.

5. CORRESPONDENCE WITH CURRENT GUIDELINES

This approach corresponds with national and international ethical guidance.

All current South African ethical guidelines endorse payment for expenses (DOH, 2004; 2006; MRC, 2001; 2003). Guidelines governing research funded by the Medical Research Council endorse additional payments for time and inconvenience (MRC, 2001), including guidelines for preventive vaccine trials endorsed by the NHREC (MRC, 2003). Department of Health guidelines appear to endorse payment of expenses (transport, food) and they allow 'financial benefit' that is fair and reasonable (DOH, 2004; DOH, 2006).

International guidelines tend to endorse payments for expenses and payments for time and inconvenience (CIOMS, 2002; OHRP IRB Guidebook, 1993; UNAIDS, 2007).

Table 1: Table of ethical guidance relating to payment

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| South African DOH (2004) <i>Structures, principles and processes</i> | 7.7. Incentives APPENDIX A | Incentives relating to <u>financial benefit, transport, and food</u> should be fair and reasonable |
| South African DOH (2006) <i>Good clinical practice guidelines</i> | 4.12 Trial incentives | Participants must be reimbursed for all reasonable <u>costs</u> related to trial participation. Incentives relating to <u>financial benefit, transport, and food</u> should be fair and reasonable |
| SA MRC (2003) <i>Guidelines on Ethics for medical research: HIV Preventive Vaccine Research (endorsed by INHREC).</i> | 10.1.1. Benefits | Participants should receive reimbursement for <u>travel</u> and <u>compensation for time and inconvenience</u> |
| SA MRC (2001) <i>Guidelines on ethics for medical research: General principles</i> | 9.13.1 Inducements to healthy volunteers | Reimbursement of <u>expenses</u> is allowed Compensation for <u>time, inconvenience</u> and <u>discomfort</u> should be paid over and above reimbursement for <u>expenses</u> |
| CIOMS (2002) | Guideline 7: Inducement to participate | Participants may be reimbursed for lost earnings, travel costs and other research-related <u>expenses</u> . Participants may be compensated for <u>time and inconvenience</u> . |
| OHRP IRB Handbook (1993) | Chapter 3 & 4 Section G: Incentives Section I: Identification and recruitment of subjects | <u>Re-imbusement</u> for travel, babysitting etc may be provided. Volunteers are compensated according to the type and number of procedures, anticipated <u>inconvenience</u> , and the <u>time</u> involved. Payment should reflect the degree of <u>inconvenience</u> associated with participation |
| UNAIDS (2007) <i>Ethical considerations</i> | Guidance point 12: Benefits | Participants should receive reimbursement for |

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| <i>in biomedical prevention trials</i> | | <p>travel and other <u>expenses</u> related to participation.</p> <p>In recognition of <u>time</u> and <u>inconvenience</u>, the appropriate levels of (and forms) the incentives take will depend on socio-economic context.</p> |
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6. APPLICATION TO CASES

It could be argued that the above approach is easiest to apply for participants who are healthy and participants who are adults.

However, the above approach may also be applied to trials with *patient-volunteers*. In such instances, RECs could consider the following questions for each element:

1. What *time* are patient-volunteers spending in research procedures (e.g. questionnaires, additional procedures?) additional to interventions/ procedures they would be undertaking as part of their care?
2. What *inconvenience* are patient-volunteers assuming from such research procedures?
3. What *expenses* are patient-volunteers assuming to take part in research activities that is additional to costs they would have assumed as part of their care? (e.g. additional visits?)

Furthermore, the above approach may also be applied to trials with *adolescent* participants. In such instances, RECs could consider the following issues:

Compensation payments for time and inconvenience should be made to the party assuming the burdens, that is, the adolescent participant. Adolescent participants could be paid a time-payment commensurate with minimum wage payment for teenagers, and such payment could be in-kind (e.g. airtime, vouchers) with modest increments for inconvenient procedures where relevant. Expense payments should be made to the party assuming the expenses.

7. SUMMARY

In summary, the proposed payment approach is payment for Time, Inconvenience and Expenses (TIE). It is clear that payment is not being proposed for human tissues or materials that participants may provide as part of their research participation.

Payment, in the form of compensation for time and inconvenience and reimbursement of expenses, is a fair way to zero out participants' costs and acknowledge the burdens they endure. Because payments are linked to other similar opportunities, and to actual expenses incurred, the potential for "undue inducement" may be lessened. That is, this approach attempts to reconcile concerns about fairness with concerns about preserving authentic informed consent.

The NHREC does not detail what rates should be attached to each component, nor an overall level of payment for trial visits. Such decisions should be left to RECs based on the specificities of the trial at hand (for example, the time spent at each visit, and the trial procedures). In

general, however, shorter visits with less burdensome procedures will have lower payment amounts than longer visits with more burdensome procedures.

RECs should consider time, inconvenience and expenses in coming to a decision as to whether a payment amount/ schedule in a given trial is fair and does not comprise an undue incentive. In coming to its decision, the REC should be able to justify a decision about payment based on the following questions (i) Is the payment reflective of Time, Inconvenience and Expenses (TIE) as outlined above and can the payment be justified as fair in a defensible manner based on these criteria? (ii) Is the payment likely to represent an appropriate incentive for participants in the particular study?

We ask RECs to hold a balanced view: While preserving authentic informed consent is critical to justifying payment, this is insufficient alone to justify payments, which must also be fair. Over time, greater consensus may emerge within and between RECs with regard to appropriate compensation for time and inconvenience for particular research procedures, and reimbursement of expenses. At present, the NHREC recommends that RECs carefully consider the issue of payment, using the considerations outlined above, on a trial-by-trial basis.

If this approach is implemented, trial payments will differ. A trial with fewer, shorter visits and less inconvenient procedures will pay participants less than one with multiple, lengthier visits and more complicated. When trial participants are paid for their actual costs, their expense payments will differ. This will require participants and participating communities to understand *what* is being paid for, in order for these differences to be understood to be fair. Arguably, both participants and participating communities are often expected to understand much more complex concepts than differential payment, such as (for example) placebo-control.

In closing, considering fair payment for research participation is a separate calculation from the multiple, varied and complex ethical calculations already undertaken by RECs when reviewing protocols. The NHREC appreciates that RECs will undertake such assessments as a matter of routine, including whether there is an appropriate balance of risk to benefit/ knowledge ratio, or whether community engagement efforts are sufficient. This document serves to provide RECs with ethical considerations to inform their review of payment for trial participation.

8. REFERENCES

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