Compensation for research-related harm: The implications of *Venter v Roche Products (Pty) Limited and Others* for research ethics committees

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Background. The issue of what type of compensation a research participant would be entitled to in a clinical trial when they have signed an informed consent document excluding certain forms of compensation recently came before our courts in the matter of *Venter v Roche Products (Pty) Limited and Others* (Case No. 12285/08). In this case, the court had to consider whether the plaintiff, Mr Venter, was entitled to claim for non-medical costs such as pain and suffering, loss of income and general damages, even though the informed-consent document expressly excluded such claims.
Objectives. To set out the facts, issues and judgment in the case, concluding with a discussion of the implications of the judgment for research ethics committees (RECs).
Methods. Critical review of a judgment of the Western Cape High Court.
Results. The court concluded that Mr Venter's application for damages should be dismissed because he had voluntarily agreed to the limited compensation as set out in the informed consent form that had been approved by both the local RECs and the Medicines Control Council.
Conclusions. The *Venter* case has shown that delictual claims for research-related injuries will not be successful if plaintiffs have agreed to limit their own rights through signing an informed-consent form that limits compensation. This places an important obligation on RECs to ensure that they carefully review compensation clauses in informed-consent documents and that these are made clear to potential research participants.

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Section 27 of the South African (SA) Constitution provides that: (*i*) everyone has the right to have access to healthcare services, including reproductive health care; and (*ii*) the state must take reasonable legislative and other measures – within its available resources – to achieve the progressive realisation of each of these rights.[1] The provision of medicine and healthcare services plays a central role in ensuring that individuals have access to quality healthcare. Given that access to effective medicines and quality healthcare services underpin this right, great value has been attached to health research which is aimed at developing medicines and improving such services.[2] The mission statement of the national Health Research Policy in SA reflects this by providing that the state must 'promote research that contributes towards the improvement of human health and welfare'.[2]

Health research frequently requires the use of human volunteers, who may bear some risk in order to generate new knowledge. Their interests are often pitted against those of science and broader public health goals.[3] As a result, a central concern in the regulation of health research is that the interests of society and of science do not override the interests of individual research participants.[4]

The issue of the interests of science and society v. those of individual research participants recently came before our courts in the matter of *Venter v Roche Products (Pty) Limited and Others* (Case No. 12285/08) (hereafter '*Venter*'). In this case, the court had to consider whether the plaintiff, Mr Venter, was entitled to claim for non-medical costs such as pain and suffering, loss of income and general damages, even though the informed-consent document that he had signed expressly excluded such claims.[5]

This article sets out the facts, issues and judgment in the case. It concludes with a discussion of the implications of the judgment for research ethics committees (RECs).

The facts of the case

In 2005, Mr Venter agreed to participate in a study on the safety and efficacy of an experimental cancer drug for the treatment of colon, breast and lung cancer (paragraphs (paras) 1 and 8 – all paragraph numbers refer to the relevant paragraphs in the *Venter* case). The study was a global one sponsored by F Hoffman-La Roche AG (FHLR), a Swiss company (para 8). FHLR entered into a written agreement with Roche SA to conduct the study on their behalf in SA (para 11). Roche SA in turn, entered into a sub-agreement with a Dr Raats at GVI Oncology in the Western Cape to act as the principal investigator and trial site (para 15).

Regulatory approval for the clinical trial was obtained from the Medicines Control Council (MCC) and two RECs, of the University of the Witwatersrand and Pharma Ethics (para 12), both of which approved the study and the informed-consent document that was to be used (para 14).

Mr Venter was invited to participate in the study by a Dr Van der Merwe from GVI Oncology. He was given a copy of the informed-consent document to read at home, and 5 days later Dr Van der Merwe went through it with him point by point (para 17). Mr Venter thereafter agreed to be a participant in the study and signed the consent form (para 17).

The consent document expressly provided that the sponsor, FHLR, would pay for the cost of medical treatment directly linked to any trial-related injury, and that no other compensation would be

available (para 3). Furthermore, any claims for compensation would be determined in line with the guidelines issued by the Association of British Pharmaceutical Industry (ABPI), on which the SA Good Clinical Practice guidelines (GCP) are based (para 3).

Mr Venter subsequently suffered a research-related injury and had to be hospitalised (paras 5 and 18). He claimed that he had suffered damages as a result of this research-related injury, and instituted a civil action against Roche SA and GVI Oncology (para 5).

Issues

Given that the informed-consent document expressly limited compensation to medical costs (para 21), in dispute was whether Mr Venter was entitled to claim for non-medical costs such as pain and suffering, loss of income, and general damages.

Judgment

The first issue before the court was determining whether a tacit contract existed between the parties in which it was agreed that compensation beyond the stipulated medical costs would be paid in the event of a research-related injury (paras 31 - 37). In this instance, the court found that there was no tacit agreement between Mr Venter and Roche SA on the issue of compensation. This was because: (*i*) in terms of the arrangement between FHLR and Roche SA, FHLR was to obtain insurance for the trial – this was in line with clause 4.11 of the GCP, which requires the sponsor to pay compensation for any trial-related injuries; (*ii*) the informed-consent document provided that FHLR, as the sponsor of the trial, was responsible for compensation and it could be assumed that the reasonable person in the position of the plaintiff would have been aware of this clause before signing; (*iii*) there was no evidence that Dr Van der Merwe or GVI Oncology had the authority to conclude a tacit agreement, or that Mr Venter intended to conclude a contract with a party not listed on the informed-consent form; and (*iv*) clause 15 of the informed-consent form contained an indemnity for GVI, for trial-related injuries (paras 40 - 42).

The second issue considered by the court was whether the wording of the compensation clause in the informed-consent document gave rise to a broader obligation to pay compensation beyond medical costs (para 43). This part was headed 'compensation' and stated that FHLR (the sponsor) would pay for the costs of medical treatment following a research-related injury. Any compensation provided would be determined in terms of the ABPI guidelines, with no other compensation being payable (para 44).

Although the court held that the term 'compensation' had a broad meaning and included compensation for loss suffered as a result of a trial-related injury, i.e. damages (para 47 - 48), it found that the informed-consent document required any compensation to be determined according to the ABPI guidelines (para 53). A review of the ABPI guidelines found a recommendation for payment without legal commitment, i.e. an *ex gratia* payment by the sponsor and not by the researchers (paras 39 and 58). The court quoted with approval the English decision of *Morton James Wylie v Dr Donald Grosset, Greater Glasgow Health Board* (2011), where it was held that the ABPI guidelines on compensation were a procedural rather than a substantive guide to sponsors (para 61). Based on the above, the court concluded that there was no legal obligation to pay compensation beyond the medical costs in Mr Venter's case (para 62).

The third issue addressed by the court was whether a *stipulato alteri* (an offer to a third party that comes into effect when the agreement is signed) existed (para 66). Mr Venter alleged that, as the MCC application stated that all regulatory requirements would be met and that the trial would be conducted in accordance with the GCP guidelines, there existed a *stipulato alteri* in favour of the trial participants (para 67). The court again rejected this, finding that there was no evidence that Mr Venter had either seen the MCC application or had intended to accept a third-party offer by signing the consent form (para 67).

The fourth issue was whether Roche SA and GVI Oncology breached a legal duty that they owed to Mr Venter. The court found that there was no evidence that Roche SA and GVI Oncology's failure to include an agreement to provide broader compensation was wrongful (para 71). In particular, the court noted that expert evidence had indicated that the MCC regularly approved studies without such compensation obligations (para 72).

In the light of the above, the court concluded that Mr Venter's application for damages should be dismissed (para 94).

Discussion

The outcome of the *Venter* matter is important, as it is our first judgment on compensation for non-medical injuries following a research-related injury. This matter has clarified the approach that the courts will take to such disputes by highlighting a number of applicable principles. Firstly, the obligation to assess and approve the nature of the compensation for research-related injuries falls on the regulators reviewing and approving the study. Secondly, participants are bound by the express terms of the informed-consent document that have been approved by these regulators, and any verbal or tacit amendments to such documents would need to be reduced to writing if they are to be enforceable.

Both these principles have significant implications with regard to the way in which RECs review clinical trials.

Role of RECs in establishing what forms of compensation for harm are ethical

The court held that regulatory approval had been obtained from the MCC and two ethics committees (para 12). All three regulatory bodies had approved the content and wording of the informed-consent document (para 14). The court appeared to accept that limiting compensation in this way was reasonable because, firstly, such bodies had the legal authority to approve/not approve research, and, secondly, this stance on compensation in this instance reflected an accepted practice in the field (para 72).

It is submitted that the court was correct in viewing the responsibility to set the normative standards for compensation as being in the hands of the regulators. The MCC must ensure that clinical trials are scientifically valid and that they comply with certain ethical standards such as obtaining consent from participants,[6,7] while RECs must grant ethical approval if a protocol is found to be ethical.[8] Compensation for research-related harm is clearly an ethical issue, which is referred to in both the national ethical guidelines[9] and the GCP.[7] This seems to imply that the MCC and RECs should ensure that adequate compensation arrangements are in place, as part of the assessment of whether health research is ethical.

However, there is limited ethical guidance on this point, and possibly there are divergent approaches in practice. Neither the national ethical guidelines[9] nor the GCP[7] set a substantive standard on compensation for harm. However, the national ethical guidelines require arrangements to 'ensure adequate compensation to participants for injury suffered as a result of participation in the trial'.[9] These arrangements must be specified in the informed-consent document,[9] while the GCP guidelines focus on the procedures and substantive standards that should be followed if there is a dispute regarding the nature of compensation to be paid.[7]

This lack of specific ethical guidance on compensation leaves open the question of whether limiting compensation to medical costs is ethical. The court found that as the regulators had approved the study with this specific limitation on the kinds of compensation that could be claimed and Mr Venter had agreed to this, he could not at a later point argue that the researchers or sponsors had acted wrongfully (para 71). This means that RECs must specifically consider the issue of the compensation standards when approving research as part of their ethical obligation to protect research participants and promote their welfare. Furthermore, members of RECs should ensure that they carefully consider the express wording of the compensation clause and that they are satisfied with it if it limits a participant's rights by excluding certain forms of damages. This is because once the informed-consent document is approved and consented to by a participant, a participant cannot argue later that the researchers or sponsors had acted wrongfully (para 71).

Implications of the express terms of the informed-consent document

Our law is clear regarding the obligation to obtain consent from research participants. The National Health Act provides that when a health service is experimental and is being undertaken at a health establishment, there is a duty on that establishment to inform the user that the service is a form of research.[8] Researchers are also required to inform research volunteers of the 'objects of the research or experimentation and any possible positive or negative consequences on his or her health'.[8] With regard to compensation, point 3.5 of the GCP provides that the informed-consent document should specify the 'compensation and/or treatment available to the participant in the event of trial related injury'.[9] In summary, these norms require information on compensation, but do not set a substantive norm on what types of compensation should be provided by sponsors.

The court made it clear that it would not recognise terms that were not expressly provided for in the informed-consent document. It is submitted that this is the correct approach from a public policy point of view, and it would be inappropriate if research participants could 'negotiate' alternative conditions under which they would participate in a study. Furthermore, the court held that as the defendant, Mr Venter, had given informed consent, this excluded wrongfulness, thus excluding the possibility of a civil claim.

The above facts and issues considered, it is submitted that RECs must ensure that researchers implement an adequate informed-consent process that brings to the attention of participants the distinction between the researchers and sponsors, and the limitation of compensation – as defined by the express wording in the consent document. Furthermore, informed-consent documents should confirm that the participant is aware that any verbal or other changes to the content of the signed consent document would only be legally binding on the researchers and sponsors if they were reduced to writing and brought to the attention of the REC concerned.

Claims in terms of the GCP

It is submitted that the court erred in so far as it viewed the GCP as being only procedural in nature and misinterpreted the role of GCP norms within the context of the wording of the specific informed-consent document.

It is considered that the guidance in the GCP is not just procedural in nature. Although it does not specifically state what forms of damages should be covered by the sponsors of research, there are two principles indicating that the drafters intended a broader approach. Firstly, they state that sponsors must obtain 'comprehensive' insurance. Secondly, they refer to the need to ensure that the amount of compensation will be 'appropriate to the nature, severity and persistence of the injury and should in general terms be consistent with the quantum of damages commonly awarded for similar injuries by a South African Court in cases where legal liability is admitted'.[9] It is argued that these are substantive rather than procedural obligations, implying that a broad approach to compensation is not excluded.

Finally, it is submitted that the wording of the informed-consent document indicated that any dispute regarding the specified compensation would be determined in terms of the ABPI guidelines. This indicates that disputes regarding issues such as whether certain medical costs could be covered would be resolved by reference to the substantive norms in the GCP – which provide that, for example, a participant may only claim for serious bodily injury of an 'enduring character'.[10] It is circular logic to state that there is no legal obligation to pay compensation beyond that set out in the GCP, as these guidelines provide that the 'fact that a sponsor has agreed to abide by these Guidelines in respect of a trial does not affect the right of a participant to pursue a legal remedy in respect of injury alleged to have been suffered as a result of participation'.[7]

Conclusions

The *Venter* case has shown that delictual claims for research-related injuries will not be successful if the plaintiff has agreed to limit his/her own rights through signing an informed-consent form that limits compensation. This places an important obligation on RECs to protect the rights and welfare of research participants by carefully reviewing compensation clauses in informed-consent documents. The national ethical guidelines require that compensation arrangements be 'adequate',[9] and in light of this, RECs should consider what is just in the circumstances. Is it in fact appropriate to limit compensation to medical costs when participants may lose earnings and endure pain and suffering and other forms of harm in the event of a serious adverse event? RECs are obligated to ensure that participants are made aware that if compensation is limited to medical costs, they will not be able to claim other delictual damages at a later stage.

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