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Human-animal neural chimera research in South Africa: Ethical concerns, regulatory gaps, and a tiered governance framework

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Background. Human-animal neural chimera research (HANCR) raises distinctive ethical concerns because human neural cells may contribute to the central nervous system of animal hosts in ways that could alter cognition, emotional capacities, behaviour or interests relevant to animal welfare and moral status. South Africa (SA) currently has no chimera-specific governance framework, despite growing international emphasis on differentiated oversight for higher-risk forms of chimera research.

Objectives. To evaluate the ethical and regulatory implications of HANCR in SA and to propose a governance response proportionate to the risks posed by different forms of neural chimera research.

Methods. This article undertakes a normative legal-ethical analysis of HANCR. It draws on international literature on chimera ethics and oversight, SA research ethics and animal research governance instruments, and applies consequentialist, deontological, and *ubuntu*-informed Afro-communitarian ethical perspectives.

Results. The analysis shows that HANCR is not ethically uniform. Ethical risk varies according to the extent and unpredictability of neural contribution, the developmental stage at which human cells are introduced, the species involved, and whether breeding or reproduction is permitted. The current SA framework is fragmented across human and animal research oversight and lacks an integrated mechanism for assessing neural chimera protocols. Although ethical concerns justify heightened scrutiny, a blanket moratorium would be broader than necessary where more tailored regulatory options are available. A tiered governance framework with integrated review, clearly defined prohibited categories, enhanced welfare and behavioural monitoring, and restrictions on breeding would better match the ethical stakes.

Conclusion. SA should move from regulatory silence to differentiated oversight of HANCR. Lower-risk forms may be reviewable under integrated and specialised oversight, while higher-risk categories should be prohibited or deferred pending explicit national criteria and appropriate review capacity.

Keywords: human-animal neural chimera research, neuroethics, research ethics, animal research ethics, South Africa, regulatory governance, moral status, *ubuntu*

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Human-animal neural chimera research (HANCR) has emerged as one of the most ethically contested areas of contemporary biomedical science. By introducing human neural stem or progenitor cells into animal embryos, fetuses or postnatal animals, researchers seek to model neurological disease, investigate brain development and, in some cases, explore future therapeutic applications.[1-5] Ethical concern does not arise simply because such research is scientifically novel. Rather, neural contribution is morally distinctive because it may alter cognition, emotional capacities, behaviour or interests in ways that bear directly on animal welfare and on judgements about moral status.[2-5] As recent reviews and oversight analyses indicate, the central ethical question is not whether all chimera research is impermissible, but whether some forms of HANCR create morally significant uncertainty that conventional research governance mechanisms were not designed to assess.[2,6-8]

Internationally, responses to this uncertainty have increasingly taken the form of differentiated oversight rather than categorical prohibition. Contemporary governance literature, together with the International Society for Stem Cell Research guidelines, distinguishes between lower-risk and higher-risk forms of chimera research by reference to such factors as the species involved, the developmental stage at which human cells are introduced, the likely extent of human neural contribution, and whether breeding or reproduction is permitted.[6-8] This shift is especially important in the South African (SA) context. SA has no statute or national guideline directed specifically at human-animal neural chimeras. Any proposed HANCR protocol would therefore have to be assessed through overlapping but separate frameworks governing health research ethics, animal research ethics and professional accountability.[9-12] Although these frameworks provide important protections within their respective domains, they do not establish an integrated mechanism for addressing the distinctive ethical and regulatory issues raised where human neural material is introduced into animal central nervous systems. The result is a genuine governance lacuna at the interface of

human research ethics committee (HREC) and animal research ethics committee (AREC) oversight.[6,7,9-12]

This article argues that SA should not approach HANCR through regulatory silence, but neither should the issue be framed as if the only alternative were blanket prohibition. The more defensible response is a tiered governance framework that recognises that not all HANCR is ethically equivalent. Drawing on consequentialist, deontological and *ubuntu*-informed Afro-communitarian analysis, the article shows why some forms of HANCR may be reviewable under integrated and specialised oversight, whereas others should be prohibited or deferred unless and until explicit national criteria and appropriate review capacity are developed. The central claim is that the SA regulatory challenge is best understood not as whether HANCR should be permitted in general, but as how differentiated forms of HANCR ought to be governed in a manner that is ethically proportionate, publicly accountable and socially responsive.

Ethical analysis

Consequentialist concerns

From a consequentialist perspective, the ethical permissibility of HANCR depends on whether its likely benefits outweigh its foreseeable harms. The standard justification for HANCR is that introducing human neural cells into animal systems may produce more informative models of neurological disease, deepen understanding of brain development, and potentially contribute to future therapeutic innovation.[1-5] However, the strength of that justification depends not merely on the possibility of benefit, but on its probability, magnitude and comparative value. As the recent literature notes, claims about the translational promise of chimera research are often expressed in broad and future-orientated terms.[1,2] Where anticipated benefits remain uncertain or remote, they cannot automatically outweigh immediate and predictable harms.

Those harms include, first, animal suffering. HANCR is ethically distinctive because it intentionally targets the central nervous system, thereby raising the possibility not only of ordinary experimental burdens, but also of changes in cognition, emotional capacities or behaviour that may intensify welfare concerns or alter the character of the harms imposed.[2-5] Secondly, there are institutional and social harms. Chimera research, especially where it involves neural tissue, is normatively charged and may generate public concern about boundary-crossing scientific practices.[6,7] In research environments that depend on public trust and institutional legitimacy, such concern is ethically significant. Thirdly, in resource-constrained settings, consequentialist analysis must also attend to opportunity costs. The allocation of scarce funding, infrastructure and review capacity to ethically controversial, high-uncertainty research may displace work offering clearer and more immediate social value.[1]

Consequentialist reasoning therefore does not support a single verdict across HANCR as a field. Lower-risk protocols with bounded welfare implications and strong scientific justification may be easier to defend than protocols involving greater uncertainty about neural contribution or species-sensitive harms. The consequence for governance is a need for differentiated scrutiny in which the strength of scientific justification, the availability of alternatives, and the scale of potential welfare and legitimacy harms are assessed proportionately.

Deontological concerns

A deontological analysis shifts attention from aggregate outcomes to moral constraints grounded in respect and non-instrumentalisation. In the context of HANCR, the central concern is that the deliberate introduction of human neural material into animal central nervous systems may create beings whose moral standing becomes less clear while they continue to be treated as instruments of research.[3-5] The ethical problem is therefore not limited to the possibility of suffering. It also concerns whether certain kinds of beings may permissibly be created and used for experimental ends when the intervention itself is directed at capacities often regarded as morally significant, such as cognition, emotional responsiveness or agency.[3,6]

This concern is sharpened by moral uncertainty. If a protocol creates a realistic possibility that an animal's capacities may shift in morally relevant ways, the risk is not merely empirical but normative. A mistaken welfare judgement within ordinary animal research may be serious; a mistaken judgement about the standing of a being whose capacities have been altered may be more serious still, because it raises the prospect of wrongful instrumentalisation.[3,6] For this reason, deontological reasoning places weight on the burden of justification. It is not enough for a protocol to promise useful knowledge. Those proposing morally boundary-testing research must show why it is permissible to proceed despite uncertainty about the status of the beings affected.[6,8]

A deontological approach therefore supports a more restrictive stance towards protocols that create substantial uncertainty about status or that risk collapsing morally important distinctions without adequate justification. Its governance implication is that some forms of HANCR may be reviewable only under heightened safeguards, while others may properly fall into prohibited or deferred categories where respect-based limits cannot confidently be maintained.

Ubuntu-informed concerns

Ubuntu-informed Afro-communitarian ethics adds a distinctively SA normative perspective to the analysis. *Ubuntu* is commonly associated with the view that persons are constituted through relationships and that moral rightness is closely tied to solidarity, mutual recognition and communal harmony.[13,14] In bioethical contexts, this framework does not displace concern for welfare or rights, but broadens ethical evaluation beyond individualised harms and benefits to include the social meaning, legitimacy and relational effects of scientific practice. In the case of HANCR, this matters because neural chimera research intentionally unsettles familiar human-animal boundaries in ways that may generate not only technical uncertainty, but also moral unease about how such beings ought to be treated.

From an *ubuntu*-informed perspective, ethically responsible science must remain publicly accountable and socially responsive. Practices that outpace the moral and institutional frameworks needed to justify them risk eroding communal trust and weakening the legitimacy of the research enterprise.[13,14] HANCR would therefore be difficult to defend where benefits are speculative, governance is fragmented, and institutions cannot explain convincingly why a particular protocol is necessary, how boundaries will be maintained, and how public trust will be protected. *Ubuntu* accordingly supports a regulatory approach that incorporates transparency, accountability,

and forms of oversight capable of sustaining ethical legitimacy, especially for higher-risk protocols.

Taken together, these three perspectives do not show that all HANCR is ethically impermissible. They do, however, show that HANCR raises distinctive concerns about welfare, moral status, instrumentalisation and social legitimacy that ordinary research review processes may not adequately capture. Those concerns vary across different forms of HANCR, and that variation supports a differentiated governance response rather than either regulatory silence or a blanket prohibition.

Scenario-based application of the ethical frameworks

The ethical force of consequentialist, deontological and *ubuntu*-informed concerns varies across forms of HANCR. Relevant variables include the species involved, the developmental stage at which human neural cells are introduced, the likely extent and unpredictability of neural contribution, and whether breeding or reproduction is permitted.[2-8] A differentiated ethical assessment is therefore necessary.

Postnatal rodent disease models

At the lower-risk end of the spectrum are postnatal rodent models in which human neural cells are introduced for limited disease-modelling purposes under controlled laboratory conditions. These studies may be easier to justify consequentially, particularly where they address serious neurological disease, use small animals with shorter developmental windows, and pursue narrowly defined scientific aims.[1,4,5] Even here, however, ethical concern does not disappear. Animal welfare burdens remain significant, and the possibility of altered behaviour or emotional functioning means that ordinary welfare assessment may be insufficient.[2-5] From a deontological perspective, the risk of morally significant status change is lower than in more developmentally extensive interventions, but it is not absent. *Ubuntu*-informed analysis likewise requires public justification and accountability even for comparatively lower-risk protocols. Such studies may therefore be reviewable in principle, but only under enhanced behavioural and welfare monitoring rather than routine animal research review alone.

Embryonic or prenatal neural integration

Ethical concern intensifies where human neural cells are introduced at embryonic or prenatal stages. At this point, the extent, location and developmental consequences of neural contribution may be less predictable, and the intervention may shape the central nervous system over a longer period of gestation or development.[4-8] Consequentially, this increases uncertainty about both welfare effects and eventual scientific value. Deontologically, the concern is sharper because these interventions more directly raise the possibility of creating beings whose morally relevant capacities may be altered in ways that are difficult to foresee or delimit.[3,6] From an *ubuntu*-informed perspective, such protocols are also more likely to provoke moral unease because they more visibly trouble established boundaries without clear public criteria for justification. These features do not necessarily require absolute prohibition in every case, but they do support heightened scrutiny, specialised review, and a strong presumption against permissibility unless the scientific rationale is compelling and the safeguards unusually robust.

Non-human primate studies

Neural chimera studies involving non-human primates raise particularly acute ethical concerns. Consequentialist reasoning becomes more restrictive because the baseline welfare stakes are already high, and any increase in cognitively or emotionally significant capacities would intensify those concerns.[2-5]

Deontological analysis is likewise more demanding because non-human primates already possess comparatively complex cognitive, emotional and social capacities that are often taken to matter morally; interventions directed at their central nervous systems therefore heighten concerns about status uncertainty and instrumentalisation.[3,6] *Ubuntu*-informed analysis reinforces this caution, since public legitimacy is especially likely to be strained where research appears to narrow the symbolic and moral distance between humans and animals already regarded as cognitively complex. These protocols should therefore be treated as high-risk categories requiring exceptionally stringent review and, in the absence of explicit national criteria and specialist review, should be prohibited or deferred.

Breeding and reproduction of chimeric animals

The strongest case for restriction arises where breeding or reproduction of neural chimeric animals is contemplated. Reproduction increases uncertainty not only about present welfare and status, but also about persistence, transmission and social meaning across generations.[6-8] Consequentialist concerns are magnified because the scale and downstream effects of the intervention become less controllable. Deontological concerns are also at their strongest, because reproduction may entrench the creation and use of beings whose standing is uncertain. From an *ubuntu*-informed perspective, permitting breeding without clear and publicly defensible boundaries would be difficult to reconcile with accountable and socially responsive research governance. For these reasons, breeding or reproduction should be treated as a red-line or, at minimum, a deferred category pending explicit national criteria.

Taken together, these scenarios show why HANCR should not be governed as a single undifferentiated field. Some lower-risk protocols may be ethically reviewable under tightly controlled conditions, while others warrant far stronger restrictions. The variation in ethical risk across these scenarios supports a tiered SA governance model rather than either blanket permissiveness or a field-wide moratorium.

SA regulatory framework

SA has no statute or national guideline directed specifically at HANCR. Any such research would therefore have to be assessed through overlapping frameworks governing health research ethics, animal research ethics and professional accountability.[9-12] Although these instruments provide important protections within their respective domains, they were not designed to address the integrated ethical questions raised when human neural material is introduced into animal central nervous systems. The central regulatory difficulty is therefore not an absence of ethics review as such, but the absence of a chimera-specific mechanism capable of addressing hybrid risks that cut across ordinary institutional boundaries.

Where HANCR uses human stem cells or other human biological material, the SA ethics in health research guidelines issued by the

National Health Research Ethics Council (NHREC) under the auspices of the National Department of Health would be implicated, and review would be likely to fall, at least in part, within the remit of a registered HREC.[9] The NHREC's role is to establish national norms and standards, determine guidelines, register and audit research ethics committees, and promote accountability in the research ethics system; it is not itself a primary protocol review body.[9] The NHREC guidelines provide a principled framework centred on scientific merit and integrity, respect, justice, care and beneficence, and they expressly recognise the need for ethical responsiveness to technological change.[9] However, they do not contain criteria tailored to chimera research. In particular, they do not indicate how committees should assess morally salient neural contribution, possible changes in animal cognition or emotional functioning, or uncertainty about the status of resulting beings. A conventional HREC may therefore be able to evaluate the sourcing and governance of human material, but is not necessarily structured to assess the full animal, neuroethical and developmental implications of HANCR.

Animal-related review would ordinarily fall to an AREC, operating within the framework of institutional animal ethics governance and relevant SA standards, including *SANS 10386:2021, The care and use of animals for scientific purposes*.[10] That standard incorporates the familiar principles of replacement, reduction and refinement and requires harm-benefit justification for animal use.[10] These are indispensable protections. Nonetheless, they are directed to conventional animal experimentation and do not directly address the distinctive questions raised where research intentionally seeks human neural contribution to the central nervous system. An AREC may be well placed to evaluate housing, procedures, endpoints and welfare protections, but less well placed to determine how uncertainty about neural contribution, cognition, behavioural change or moral status should affect ethical permissibility.

The practical result is a dual-review problem. A protocol involving HANCR may require both HREC and AREC scrutiny, yet neither committee, operating alone, is intrinsically equipped to evaluate the integrated ethical stakes of the protocol.[6-10] Nor does the current SA framework appear to require a joint review process, a specialised referral pathway, or nationally standardised criteria for neural chimera protocols as such. The absence of an integrated or specialised review mechanism creates the risk of fragmented assessment, inconsistent thresholds, and uncertainty about where responsibility lies for evaluating morally significant neural effects that are neither purely human research issues nor purely animal welfare issues.

Broader professional and regulatory guidance reinforces the need for stronger governance, but does not resolve this interface problem. The Health Professions Council of South Africa's ethical guidelines for health researchers emphasise that researchers owe duties not only to participants, but also to animals, society and the research community.[11] Similarly, *South African good clinical practice*, while directed principally at clinical trials, reflects a wider expectation of rigorous oversight, institutional accountability and proportionate review in ethically complex biomedical research environments.[12] These instruments support the view that ethically novel research requires more, not less, careful governance. They do not, however, establish substantive criteria or review architecture specific to HANCR.

The SA regulatory position is therefore best understood as one of partial coverage but inadequate integration. Existing frameworks supply important ethical principles and procedural safeguards, yet they do not provide a coherent mechanism for distinguishing between lower- and higher-risk forms of HANCR or for assigning responsibility for the neuroethical questions that define the field. That governance lacuna does not justify regulatory silence. Rather, it supports the need for a more explicit, tiered oversight model capable of integrating HREC and AREC expertise, identifying red-line categories, and matching review intensity to the moral stakes of different forms of neural chimera research.

Constitutional and international law implications

Any SA response to HANCR must also be defensible in the light of legal protections for scientific inquiry. Section 16 of the Constitution protects freedom of expression, including 'academic freedom and freedom of scientific research'.[15] That protection is not absolute. Rights in the Bill of Rights may be limited under section 36, which requires that restrictions be reasonable and justifiable, taking account of less restrictive means.[15] In the present context, the relevance of this constitutional framework is not that HANCR must be left unregulated, but that limitations on research require principled justification and should not extend further than necessary to address the ethical concerns at stake.

A similar caution appears at the international level. Article 15 of the International Covenant on Economic, Social and Cultural Rights recognises both the right to enjoy the benefits of scientific progress and the duty of states to respect the freedom indispensable for scientific research.[16] General Comment No. 25 confirms that scientific freedom may be regulated, but that restrictions should be justified, proportionate and responsive to the rights and interests involved.[17] These commitments do not preclude regulation of ethically controversial science. They do, however, support the view that governance should be carefully tailored to legitimate aims, including the protection of welfare, dignity and public accountability.

For present purposes, the legal implication is limited but important. Once it is accepted that HANCR is ethically heterogeneous, a blanket moratorium becomes harder to justify than a differentiated system capable of distinguishing lower-risk from higher-risk protocols. A tiered framework with integrated review, clearly defined prohibited categories and proportionate safeguards is therefore easier to defend than a field-wide suspension, both ethically and legally. The comparative defensibility of a tiered framework does not eliminate the case for strong restriction in respect of certain forms of HANCR. It does suggest, however, that the least restrictive response consistent with legitimate ethical protection should be preferred.

Towards a tiered SA governance model

The preceding analysis suggests that the central SA policy problem is not whether HANCR should be permitted or prohibited in the abstract. The more useful question is how different forms of HANCR ought to be governed in a manner proportionate to their ethical stakes. A defensible response should therefore move beyond undifferentiated treatment and adopt a tiered governance framework that distinguishes protocols by risk, integrates relevant forms of expertise, and identifies categories of protocol that should not proceed without explicit national standards.[6-10,15-17]

Risk-based categorisation

An SA framework should begin by classifying HANCR protocols according to factors already shown to be ethically significant, namely the species involved, the developmental stage at which human neural cells are introduced, the likely extent and unpredictability of neural contribution, and whether breeding or reproduction is contemplated.[2-8] At the lower end of the spectrum would be tightly bounded postnatal rodent studies with limited and monitorable neural contribution. At the higher end would be embryonic or prenatal interventions with uncertain developmental effects, non-human primate protocols, and studies permitting breeding or reproduction. The point of categorisation is to ensure that review intensity and regulatory safeguards match the moral significance of the protocol rather than treating all HANCR as ethically equivalent.

Integrated and specialised review

Given the hybrid character of HANCR, ordinary parallel review by HRECs and ARECs is unlikely to be sufficient.[6,7,9,10] SA should therefore require integrated review for neural chimera protocols, either through formal joint review between institutional committees or through a specialised referral mechanism that brings together expertise in stem cell science, developmental biology, neuroethics and animal welfare. For higher-risk protocols, the system should operate under nationally standardised criteria developed through NHREC norms and standards, with institutional committees applying those criteria in appropriately constituted review processes.[9] This process would promote consistency across institutions.

Prohibited or deferred categories

A tiered model should also identify categories that should be prohibited or, at minimum, deferred pending explicit national criteria and sufficient review capacity.[6-8] These should include neural chimera protocols involving non-human primates beyond narrowly defined limits, protocols with a realistic prospect of extensive or poorly bounded central nervous system humanisation, and protocols permitting breeding or reproduction of neural chimeric animals. Such restrictions are justified not because every feared outcome is empirically likely, but because these categories concentrate the strongest concerns about welfare, moral status uncertainty, instrumentalisation and public legitimacy. In the absence of clear national standards, permitting such work through ordinary institutional discretion would be difficult to defend.

Enhanced monitoring, accountability and public justification

For protocols that are permitted, oversight should extend beyond initial approval. Neural chimera studies should be subject to enhanced behavioural, cognitive and welfare monitoring suited to the species and the nature of the intervention.[2-5,10] Researchers should be required to specify humane endpoints, monitoring indicators and stopping rules in advance, particularly where unexpected changes in behaviour or emotional functioning may indicate ethically significant effects of neural contribution. Breeding or reproduction should not be permitted by default; any proposal involving reproduction should be treated as presumptively impermissible unless expressly justified under nationally articulated criteria.[6-8]

An SA framework should also incorporate public accountability. *Ubuntu*-informed ethics highlights that the legitimacy of controversial science depends not only on technical compliance, but also on intelligible public justification, relational responsibility and social responsiveness.[13,14] For ethically sensitive HANCR, this need not entail public participation in every protocol decision, but it does support greater transparency about governance criteria, institutional accountability for decisions, and, where appropriate, public or community engagement on the ethical boundaries of the field. Such measures would help ensure that governance of HANCR is not experienced as a purely technocratic exercise, but as part of a broader commitment to responsible science in a constitutional democracy.

Taken together, these measures would move SA from fragmented oversight towards a more coherent governance model for HANCR. Lower-risk protocols could be assessed under integrated and proportionate safeguards, while stronger restrictions would apply where ethical uncertainty and moral stakes are greatest. That approach is more responsive to the differentiated nature of HANCR than either blanket permissiveness or blanket prohibition.

Conclusion

HANCR raises genuine ethical and regulatory concerns in SA, particularly where human neural contribution may affect animal welfare, cognition or moral status, and where the research may affect the social legitimacy of scientific practice.[2-7,9-12] The central difficulty is not simply that HANCR is controversial, but that existing SA governance frameworks were not designed to address the hybrid risks that arise at the intersection of human research ethics and animal research ethics.[9-12] At the same time, the ethical heterogeneity of HANCR[2-8] together with constitutional and international proportionality considerations[15-17] makes an undifferentiated response difficult to justify.

The more defensible approach is therefore a tiered governance framework. Lower-risk protocols may be reviewable under integrated and specialised oversight, while higher-risk categories, particularly those involving embryonic or prenatal neural integration, non-human primates, or breeding and reproduction, should be prohibited or deferred pending explicit national standards and appropriate review capacity.[6-10] SA should move from regulatory silence to differentiated oversight that is ethically proportionate, publicly accountable and socially responsive.

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