New IOM report assesses oversight of clinical gene transfer protocols

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In most cases, human gene transfer research is no longer novel or controversial enough to require additional review from the National Institutes of Health's Recombinant DNA Advisory Committee, known as RAC, says a new report by the Institute of Medicine. Patient safety is always paramount, the report says, but most individual RAC reviews no longer provide benefits beyond the existing regulatory and oversight framework and may be impeding scientific advancement with unnecessary administrative burdens.

However, NIH should consider developing a process – using RAC as a model – to rigorously review research on humans in any scientific realm that uses applications from emerging technologies or techniques that pose unknown or significant risks.

"The government's role in research must be, first and foremost, to safeguard the rights, dignity, and health of human subjects, while also facilitating vital scientific research to prevent and treat major health threats," said Lawrence O. Gostin, university professor at Georgetown University Law Center and chair of the committee that wrote the report. "The RAC has instilled public confidence in an area of research that was once deeply controversial, and the RAC model could serve as a method for transparent engagement and review of any novel scientific research that poses unknown or heightened risk."

Human gene transfer research involves the introduction of genetic material into a human subject for diagnostic or therapeutic purposes.

Individual gene transfer research protocols – extensive written research plans—currently must be reviewed by the U.S. Food and Drug Administration as well as by multiple oversight bodies at individual research institutions. Each protocol for NIH-funded research is also reviewed by RAC, which then selects a small number of potentially controversial or novel research protocols for further oversight and public review. The RAC no longer directly regulates human gene transfer research but instead advises NIH on protocols and provides a public forum for discussing scientific, technical, and ethical considerations.

Since RAC was formed in the 1970s, decades of extensive clinical and research experience have helped alleviate many of the initial concerns about human gene transfer research. Hundreds of clinical trials – predominantly Phase I clinical trials designed to evaluate safety – have been completed and much has been learned about how to ensure the safety of research participants. In addition, the promise of more effective treatments for devastating and debilitating diseases has increased the public's positive perceptions of this research.

RAC should only review individual research protocols in exceptional cases, the committee concluded. The report identifies specific criteria that a research protocol should meet before it is determined to require RAC review, such as when a new vector, genetic material, or delivery method is first used on human subjects, and when protocols cannot be adequately reviewed by other oversight and regulatory bodies. The NIH director should consult with other regulatory and oversight authorities to determine whether RAC review is warranted. But even if proposed research doesn't meet these criteria, the director should have the flexibility to select research protocols for RAC review that may present significant societal or ethical concerns.

In addition to gene transfer, other emerging technologies to be used in human research, such as nanotechnology, could benefit from public

discussion and oversight, the report says. The NIH director should convene an ad hoc working group to consider whether providing oversight and a venue for public deliberation similar to RAC for research on humans involving other emerging applications is needed. The report notes that such oversight and review should focus only on cases that have generated significant public concern or that fall outside existing regulatory capacities.

The study was sponsored by the National Institutes of Health. Established in 1970 under the charter of the National Academy of Sciences, the Institute of Medicine provides independent, objective, evidence-based advice to policymakers, health professionals, the private sector, and the public. The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council make up the National Academies. A committee roster follows.

Provided by National Academy of Sciences