of the community, the political context and the barriers — structural and behavioural — to applying the lessons that might be learned. The researchers would also need to learn how colleagues from other disciplines approach the issues and frame the research questions in a mutually acceptable way. They must also learn to respect what is possible in each discipline, and how insights are gained and possible implementations are made. All this is easier said than done, but it is essential.

Funders must rise to the challenge of supporting these tough research necessities. That means having enough of an overview of a project to oversee the selection of peer reviewers whose individual perspectives will inevitably be narrower than those of the project. An ideal funder would also include potential users of the project's outcome among its assessors, to ensure that the research has practical impact as well as academic weight.

The world is ill-equipped to uphold such ideals. For example, a paper published in this issue of *Nature* (R. Bromham *et al. Nature* **534,** 684–687; 2016) provides evidence that multidisciplinary research is less attractive to funders than single-discipline research. The work is based on an analysis of grant applications to the Australian Research Council, but there is every reason to believe that the conclusion can be generalized. The metrics of interdisciplinarity introduced by the authors can also serve as warning indicators for funders, telling them when they need to take special measures to do a project justice.

The good news is that many funding agencies are aware of the challenge, and of how far they need to go to meet it. The Global Research Council (GRC) is a forum in which government funders discuss their common challenges. At its annual meeting in Delhi last month, the focus was on interdisciplinarity. The council commissioned a survey and analysis of the practices of many funders. It also issued a statement of principles on interdisciplinarity (go.nature.com/290mqqt).

The GRC is not a decision-making body. But it was evident at the meeting that the funders recognize the need for new measures. An obvious one is that grants should last long enough for interdisciplinary research to take shape. Another is that funding agencies should have a good enough grasp of the subject matter to ensure that a well-informed, multidisciplinary assessment can be conducted.

Journals, too, must face up to such challenges. *Nature* and its research journals take pride in their capacity to handle interdisciplinary research. The multidisciplinary editorial teams see it as part of their job to do so — in selecting referees from diverse disciplines, and in considering their comments within the framing of the paper under discussion, rather than that of the individual assessors. In such a context, it is not unknown for *Nature*'s editors to overrule all referees' recommendations against publication of a technically valid paper, and to publish it.

"The good news is that many funding agencies are aware of the challenge."

What is more, the Nature journals are recruiting social scientists to address our editorial goal of increasing the attention given to the societal challenges of sustainability and health. *Nature* itself will soon be recruiting social-sciences editors. In launching *Nature Climate Change* and *Nature Energy*, and as we recruit for the launch of *Nature Human Behaviour* next year, we have already learned some important lessons about the sense of professional identity of sociologists, anthropologists, economists and psychologists.

Without that developing sense of respect for diverse types of quantitative and qualitative research, progress by funders, publishers and universities in interdisciplinary research will founder. ■

Calculated risks

Gene-therapy trials must move forward, but not without due consideration of the dangers.

Jesse Gelsinger was 18 and healthy when he died in 1999 during a gene-therapy experiment. He had a condition called ornithine transcarbamylase deficiency (OTC), but it was under control through a combination of diet and medication. Like others with the disorder, Gelsinger lacked a functional enzyme involved in breaking down ammonia, a waste product of protein metabolism that becomes toxic when its levels become too high. The gene therapy that he received used a viral vector to introduce a normal gene for the enzyme.

Gene therapy remains an obvious route to treat OTC. Simply adding the missing gene has been shown to repair metabolism in mice. But the memory of what happened to Gelsinger has slowed progress in gene therapy for any condition.

That memory was firmly on the agenda at a meeting of the US National Institutes of Health's Recombinant DNA Advisory Committee (RAC) last week. The RAC evaluates proposals to use modified DNA in human trials, and presenting to it were Cary Harding, a medical geneticist at Oregon Health and Science University in Portland, and Sam Wadsworth, chief scientific officer at Dimension Therapeutics in Cambridge, Massachusetts. The duo were proposing the first new trial of gene therapy for OTC.

Harding and the researchers at Dimension argue that the technology and our understanding of physiology have advanced enough since 1999 to try it again in people. Gelsinger died after his body overreacted to the vector used to introduce the OTC gene. Dimension's therapy uses a different viral vector, called AAV8, which has been tested numerous times in people with other conditions, with few adverse effects.

Such assurances were not enough for the RAC, and particularly not for its bioethicists and historians. Dawn Wooley, a virologist at Wright State University in Dayton, Ohio, pointed out that an RAC panel raised concerns about Gelsinger's trial in 1995, but decided to let the test go ahead. "We can't let it happen again, we cannot," she says.

Perhaps the greatest indication of how Gelsinger's death haunts the RAC came when one member suggested that the researchers explain in the consent form to be sent to prospective participants that someone had died in a similar study and attracted media attention.

There are some scientific reasons to be careful. AAV8 can cause mild liver toxicity in healthy people, and the steroids used to treat that could lead to complications in people with OTC. With so little known about these effects, the RAC members suggested that the researchers lower the dose to one that is more likely to be safe, even if it is potentially not effective.

After some discussion, the RAC voted unanimously to approve the trial. However, that came with a long list of conditions, including that the treatment first be tested in a second animal species. The researchers disagree with most of the conditions, believing that more expensive animal trials will add nothing. They feel that they are being held to a different standard from most trials.

Dimension still plans to submit an application to the US Food and Drug Administration (FDA) later this year to start a clinical trial. It is unclear how heavily the RAC's recommendations weigh into FDA decisions, but Wadsworth says that the company will conduct its trials overseas if necessary. "These patients have been waiting a long time," he says.

He is right. Therapies can be tested in non-human animals only for so long — at some point, volunteers such as Gelsinger must step forward. Yet the echoes of a trial done 17 years ago cannot be easily silenced. In fact, Gelsinger's name came up several times at the RAC meeting. Researchers from the University of Pennsylvania in Philadelphia had even mentioned him earlier that morning, when proposing the first human trial of CRISPR gene-editing technology as a treatment for cancer. The RAC approved that proposal, but its implication was clear: take care. Avoidable failures could stymie CRISPR research for decades. History must not repeat itself. ■