Non-expert nation

Scientists — just like everybody else — have little idea what will happen now that the United Kingdom has voted to exit the European Union.

Psychologists who have studied the peculiar phenomenon of buyer regret — the second thoughts that follow the purchase of a shiny new car, say — note a curious paradox. The more effort that consumers put into making their decision, the more information they seek and the more they weigh up the options, the more likely they are to want to change their mind later.

Just how much careful thought the people of the United Kingdom put into last week’s decision to quit the European Union is currently a matter of some debate. But if the prominent examples of buyer regret among people who voted ‘Leave’ and now want to ‘Remain’ are any guide, it may have been more than many critics think.

Psychologists might conclude that Kelvin Mackenzie, the former editor and now columnist of The Sun newspaper, must have been weighing up the options very carefully indeed when he wrote his “10 reasons why you must vote Brexit” the week before the crucial vote. How else to explain his U-turn, a few days after 52% of voters heeded his demand, when he admitted: “I have buyer’s remorse. A sense of being careful what you wish for. To be truthful I am fearful of what lies ahead.”

Scientists in the United Kingdom and elsewhere share his anxiety and fear. Hundreds have responded to calls from this journal to express their feelings, and the overwhelming question that they have replied with is: what happens now?

UK politicians who pushed for the country to exit the EU have gone to ground. A similar silence reigns in the European Commission’s research directorate. Commission sources munter darkly, and only off the record, of ‘uncharted territories’ and ‘needing time’ to consider the many issues that will arise. UK politicians and the research directorate declined to engage before the vote with the ‘what if’ question, at least publicly. So it is no surprise that scientists have been left with the feeling that no one had planned for the Brexit eventuality. What will be the status of those from other EU countries doing their PhDs or postdoctoral research in the United Kingdom? What will happen to the EU-funded research collaborations that are led from the United Kingdom?

What do we know for sure? Some of the most familiar European research facilities are not creatures of the EU, so will remain fundamentally unaffected by Brexit. These include the European particle-physics laboratory CERN, the European Molecular Biology Laboratory and the European Space Agency.

More recently, the European Commission has found a way to steer the creation of other, much-needed Europe-wide research infrastructures through an umbrella structure known as Instruct (European Strategy Forum on Research Infrastructures) that helps to foster intergovernmental agreements in which it has no fundamental role.

Some research infrastructures are based on a particular legal framework that stipulates that the host country must be a member state. For the European Spallation Source, headquartered in Sweden, and the Biobanking and BioMolecular resources Research Infrastructure headquartered in Austria, nothing changes. For the European Social Survey and the structural-biology infrastructure known as Instruct, both headquartered in the United Kingdom, Brexit means that new arrangements will have to be made; internal talks have already begun.

Talks on similar agreements for core European Commission scientific activities won’t start until the United Kingdom formally declares its exit by triggering the much-discussed article 50 of the EU treaty. When (and if) that will happen depends on how quickly the country resolves various questions of its own: not least, who the next prime minister will be, the proper legal route, and the broader constitutional question of whether it should follow through on a democratic decision that seems likely to damage the prospects of so many who voted for it.

If the United Kingdom does trigger article 50, research facilities owned by the commission and stationed in the country, such as the nuclear-fusion facility JET, face an uncertain future. And until a new agreement is made, UK scientists will be shut out of the EU’s multi-billion-euro Horizon 2020 programme — including its prestigious European Research Council granting body, from which the United Kingdom benefits more than any other country, by a wide margin.

Michael Gove, a senior figure in the Leave camp, notoriously claimed during the campaign that the United Kingdom has “had enough of experts”. He has got his wish, but he should beware: buyer regret is not available to those who did the selling. ■ See News p.597

The big picture

Interdisciplinary research is vital if we are to meet the diverse needs of modern society.

To tackle society’s challenges through research requires the engagement of multiple disciplines. For two examples, in responding to the challenges of climate change and of social progress, see the Comment articles on pages 613 and 616, respectively.

To highlight the issues that arise in such research, imagine an integrated project to determine the causes of destructive risk-taking in inner-city adolescents and to identify appropriate interventions. Such a programme might combine disciplines ranging from anthropology, sociology, psychology, law, economics and ethics to psychiatry, health systems, urban design and developmental neurobiology.

To frame the research challenge, and to design interventions that will be effective in targeted neighbourhoods, academic researchers need to work with non-academic partners to understand the needs
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 outcomes 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* (L. 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.

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.

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

Calculated risks

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

J esse 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.