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Drug approval needs help

It's time for researchers to lend their expertise to expediting the arrival of cutting-edge therapies that are waiting in the wings.

Funders, institutions and this publication have encouraged more scientists to get stuck into translational research. Studies that link laboratory work to clinical progress are essential if society is to benefit. Now scientists must step up again: this time, to help regulators assess and license the therapies that such projects produce. For although cutting-edge discoveries in the lab offer the potential for new treatments, they also present regulatory headaches. They have produced, for example, viruses engineered to insert a gene into cells of the retina to fight genetic disorders that cause blindness, and therapies based on gene-editing technology that alter genomes with the precision of a skilled tailor.

Take the US Food and Drug Administration (FDA), which because of the lucrative market it guards is often the first to encounter new problems. On 12 July, FDA advisers discussed a cancer therapy, based on a patient's own engineered immune cells, that has produced remarkable results in young people with leukaemia. The advisers hailed the therapy — called tisagenlecleucel and made by Novartis of Basel, Switzerland — as an important advance, and unanimously agreed that its benefits outweigh its significant risks. The FDA proper must now decide whether to approve it.

The FDA holds many such meetings of its advisers each year, but this one was unique. Usually, the committees — a mix of statisticians, clinicians, scientists and patient advocates — pick over safety and efficacy data, debating statistical details and clinical-trial design. But when it came to tisagenlecleucel, half of the meeting was spent discussing how the therapy is manufactured.

This example offers a glimpse of the regulatory complexity that cutting-edge therapies present. When a treatment is based on a person's own cells, how can the manufacturer ensure that each dose is as safe and potent as the last? Or when a treatment involves a virus, how can a company ensure that it will be safe over the long term, will not develop the ability to replicate and will not, itself, cause cancer?

The FDA does not have the in-house expertise with which to address these types of question. It needs academic scientists to get involved. There are ample ways for them to do so. For example, the FDA has set up centres of excellence involving collaboration with academic institutions.

Academics have traditionally shown little taste for the dry details of drug development, and many perceive the FDA as not engaging with the latest science. The US Government Accountability Office noted last year that the FDA has invested heavily in expanding its scientific expertise. But its report also expressed concerns that the agency has not provided clear targets by which to benchmark its efforts.

On top of this is the FDA's legendary struggle to retain its employees in highly competitive job markets. FDA commissioner Scott Gottlieb has launched a pilot programme aimed at making the agency more competitive by speeding up its recruitment process. But the FDA will need more than that to remain effective in the face of future challenges. As the agency delves into new science, a continuing dearth of expertise will become only more painful.

Some upcoming therapies that will land on FDA desks touch on the hottest fields in biomedical research. At the 12 July meeting, researchers emphasized how future research could optimize more therapies. Scientists should offer the FDA and other regulators the help to assess them. ■

Lost dimension

A flaw in the SI system leaves physicists grappling with ambiguous units.

Water is a precious resource. So protest erupted when, last September, India's Supreme Court ordered Karnataka state to release 15,000 cusecs (cubic feet per second) of the stuff per day to its downriver neighbour, Tamil Nadu. But what irked keen-eyed scientists was the nonsensical nature of the order. Cusec is a rate of flow, analogous to speed, not something that can be done "per day". Taken literally, the order was meaningless.

Dimensional analysis is supposed to prevent such errors. This involves calculating units in their own equation, for example dividing metres by seconds to get the unit for speed: metres per second. It's a handy way to sanity-check an answer — and shows that the quantity in the above court order is akin to acceleration, rather than rate or volume.

But such an analysis can come a cropper in the face of quantities that do not have dimensions such as length or time — including radians (the ratio of the length of an arc of a circle to its radius) and anything countable, such as a number of atoms. The issue arises because the International System of Units (SI) allows combinations of only seven basic dimensions and their units (such as length in metres), and allocates quantities with no extent in these dimensions a unit of '1'. That makes life simple, but hides crucial information. For example, a turning force, torque, is often measured in joules per radian. In dimensional analysis, that confusingly becomes joules, the same unit as energy. Hertz — cycles per second — reduces to 'per second', just like the frequency of non-periodic events.

Informally, physicists get around this by explicitly including the extra information. But software struggles to do that in a consistent way, and the inability to deal with this quirk formally is irksome.

Solutions exist. For example, radians could be made a new SI unit, and the unit 1 could be formally coupled with notation that includes the type of quantity that it represents. The SI system is nifty, but its real beauty is its coherence. Avoiding nonsense may require forgoing brevity for clarity. ■