Belgium. "The climate for precision breeding in general and CRISPR in particular has worsened after the ECJ ruling."

SCIENTISTS GET VOCAL

Scientists are also making public demands for exemptions from the ruling, which they say is not in line with scientific evidence. On 24 October, 170 European scientists from 75 research centres in more than a dozen countries released a position paper urging that the law should change so that crops with small DNA adaptations made through gene editing would follow the regulations for varieties produced through conventional methods such as selective breeding, not for GM organisms.

In August, the organizers of the International Plant Molecular Biology congress in Montpellier, France, started an online petition calling for a review of the ruling. The petition has now attracted more than 5,200 signatures, including Inzé's. It declares that there is "no scientific rationale" for the ruling and that the EU should regulate crop genetic techniques on the basis of science.

And on 13 September, researchers from 33 UK science, farming and agricultural–technology organizations sent an open letter to the UK government to encourage recognition of gene editing as a non-GM method.

Outside Europe, Alexandre Garcia, who heads soya-bean research and development at the Brazilian plant-breeding company Tropical Melhoramento & Genética, says that the company had been expanding partnerships and investing in several research initiatives in soya-bean gene editing, but now needs to factor in the extra compliance work needed to meet the EU rules.

"For at least the past six years, the European Union has been the second biggest market for Brazilian soya beans, and Brazil is the main provider to the EU — so if any farmer plans to plant soya beans on Brazilian land, they need to worry about EU rules," he says.

Garcia says that the decision was a "cold water bath" on the company's research activities, and that research partnerships and investments that it valued at millions of dollars are now on hold while their viability is evaluated. The company might permanently cull research projects involving gene-editing unless they are expected to recoup the higher regulatory costs, he says.

The Belgian start-up faces similar challenges. It had wanted to use CRISPR technology to develop an edible banana that is resistant to Panama disease and black Sigatoka, two fungal pests that put 80,000 African growers at risk of losing their entire crops.

Biotech entrepreneur Roel Sterken, who leads the business side of the project, says that the company had secured venture capital financing of more than €1 million (US$1.14 million), and a distribution partner. Then, within days of the July ruling, Sterken says, the finance "blew up" and the partner backed out. He attributes this to fears that consumers would conflate the new product with the bad press that GM organisms receive.

Legal experts say that there is no mechanism for appealing the European court's ruling. "We have reached the end of the road as regards the ruling," says Julian Hitchcock, a partner at the London-based law firm Marriott Harrison. The only way to reverse the decision would be for the European Commission to revise the legislation and get it passed in parliament, he says. But he adds that the commission has been sluggish in responding to rapidly changing gene-editing technologies. ■

ORGANIC CHEMISTRY

Atomic structures solved in minutes

Cross-disciplinarity led to method's use on small molecules.

BY MATTHEW WARREN

Organic chemists, make sure you're sitting comfortably. The structure of small organic molecules, such as those used in drugs, can be deduced in minutes rather than weeks, thanks to a technique that uses beams of electrons.

Three-dimensional electron diffraction has been used by some inorganic chemists and materials scientists since the mid-2000s. But organic chemists, for whom the implications could be transformative, have not adopted it widely. In mid-October, two papers[1,2] appeared online describing a way to use the technique for drugs, making it much faster and easier to work out the structures of these small organic molecules than has been possible with previous techniques.

"I think there are a lot of people smacking their heads, saying, 'Why didn't we think to do this earlier?'" says John Rubinstein, a structural biologist at the University of Toronto in Canada who uses related techniques to study large molecules. Existing methods for determining the structure of small molecules require scientists to grow crystals for analysis, a laborious process that can take weeks or months. "Something that was a real barrier to their research is now basically removed," says Rubinstein.

Knowing how atoms are arranged in a molecule is necessary for understanding that substance's function. Chemists working to develop new drugs, for example, depend on this structure to understand how a compound acts in the body — and how it could be tweaked to bind more strongly to its therapeutic target or to reduce side effects.

"I think there are a lot of people smacking their heads, saying, 'Why didn't we think to do this earlier?'"

X-ray crystallography has been used for decades to deduce this arrangement. But it can take weeks of work — and is not always successful. First, scientists need to coax the molecules to crystallize. Then they blast the crystal with an X-ray beam. The crystal's lattice structure causes the X-rays to diffract, and a detector records the resulting pattern. Scientists then use software to analyse the pattern and work out the structure of the molecule.

The challenges arise because X-ray diffraction works only with large crystals, and these can take months to form. And some molecules are so hard to crystallize that it might not even be possible to analyse them in this way.

One alternative is to replace X-rays with electron beams, which can produce diffraction patterns for much smaller crystals. In 2007 and 2008, respectively, crystallographers at the Johannes Gutenberg University in Mainz, Germany, and at Stockholm University developed the first methods for detecting the 3D structures of molecules automatically using electron diffraction[3,4]. Previously, scientists had to laboriously merge multiple 2D diffraction patterns to get this 3D structure.

Initially, the technique was used mainly with inorganic structures, which are less affected by radiation than are organic molecules. Then, in 2013, Tamir Gonen, a structural biologist at the University of California, Los Angeles, developed a version of electron diffraction called MicroED, which could be used on large biomolecules such as proteins[5].

Now, Gonen's team and another group, based in Switzerland, have shown that electron diffraction can also be used to work out the structure of smaller organic molecules. It's an important demonstration of just how fast and easy this kind of analysis can be, says Xiaodong Zou, a structural chemist at Stockholm University.

A team led by crystallographer Tim Grüne at the Paul Scherrer Institute in Switzerland

reports the creation of a prototype device for finding the structure of small molecules, using the beam from an electron microscope and a compatible detector[1].

TRIVIAL BUT TRANSFORMATIONAL

The diffraction patterns are analysed by software that is already used in X-ray crystallography. "Everything is composed of parts which have existed before," says Grüne. "It's just really the smooth integration of the system." His team used its set-up to find the structure of the painkiller paracetamol from minuscule crystals formed of the powder used inside capsules. These crystals were just a few micrometres long — much smaller than can be analysed using X-ray diffraction.

And Gonen's group adapted the MicroED technique to solve the structure of small molecules instead of proteins[2]. Gonen says that making this shift was "trivial". The main tweaks concerned the preparation of the samples, he says: whereas fragile proteins need to be treated with care, in this case, all he had to do was grind down pharmaceutical powders. The team used this adapted version of MicroED to find the structure of powders of pharmaceuticals including ibuprofen and the anti-epileptic drug carbamazepine.

These crystals were some 100 nanometres wide — a billion times smaller than those required for X-ray crystallography — and their structure could be resolved in under 30 minutes.

Rubinstein says it's surprising that a technique already used in other fields hasn't yet been widely adopted by organic chemists. "It's this great solution that's been sitting almost in plain sight," he says.

Gonen puts the oversight down to a lack of communication between disciplines. It was only when he began speaking to chemists, he says, that he became aware that they struggled to grow large crystals in order to analyse small molecules, leading him to realize he had a solution for them. "As a protein crystallographer, I never really thought very carefully about small molecules," he says. "For us, small molecules are the things we try to get rid of." ■

1. Gruene, T. *et al. Angew. Chem. Int. Edn* http://doi.org/cvw3 (2018).
2. Jones, C. G. *et al.* Preprint at ChemRxiv http://doi.org/cvvh (2018).
3. Kolb, U., Gorelik, T., Kübel, C., Otten, M. T. & Hubert, D. *Ultramicroscopy* **107**, 507–513 (2007).
4. Hovmöller, S. Electron Rotation Camera. Patent WO/2008/060237 A1 (2008).
5. Shi, D., Nannenga, B. L., Iadanza, M. G. & Gonen, T. *eLife* **2**, e01345 (2013).

FACILITIES

Himalayan observatory close to resurrection

Negotiations with Italian funding agency foster hope for climate station's future.

BY LOU DEL BELLO

Scientists hope that a Himalayan climate observatory that had its funding cut four years ago could be back in action by early next year. Managers of the Nepal Climate Observatory-Pyramid station say they are close to reaching an agreement with the Italian National Research Council (CNR). The council helped set up the station near the base of Mount Everest in 2006 but stopped funding it in 2014 because of how its budgets were managed.

"For the first time in four years, I am extremely optimistic about the fate of the station," says philanthropist and climber Agostino Da Polenza, who heads the Ev-K2-CNR Association, a non-profit group that promotes research in mountain areas and helped to set up the Nepal Climate Observatory-Pyramid, one of the highest climate observatories in the world.

If the deal goes through, the observatory will resume collecting data on atmospheric processes at high altitudes. Climate researchers say these measurements are crucial for understanding how pollution influences climate patterns.

EVK2CNR

The Nepal Climate Observatory-Pyramid is located near the base of Mount Everest.

HOPE IN THE HIMALAYAS

Da Polenza says that a meeting in October between the Ev-K2-CNR Association and the CNR to discuss the observatory's future was overwhelmingly positive, and he hopes that, come March, technicians will be on their way to the station to switch on its instruments. But he declined to reveal any further details, saying he did not want to jeopardize a potential deal before it has been finalized.

Antonello Provenzale, acting director of CNR's Institute of Geosciences and Earth Resources in Pisa, which manages funding for infrastructure, says that it is too early to disclose details of the observatory's fate, but there is a strong motivation to reinstate funding. "We all feel strongly that the Pyramid must resume activities."

The Nepal Climate Observatory-Pyramid is part of the Global Atmosphere Watch (GAW) network, run by the United Nations World Meteorological Organization in Geneva, Switzerland. The programme ▶