

they may surreptitiously degrade into other compounds that have different properties, or contain impurities that have their own biological activity.

Chemists call these irritants PAINS (pan-assay interference compounds) — and curcumin is one of the worst. “Curcumin is a poster child for these promiscuous molecules that come up often in screens,” says James Inglesse, who directs assay development and screening technology at the National Center for Advancing Translational Sciences in Bethesda, Maryland. “A lot of people doing this kind of work aren’t technically aware of all the issues that this thing can cause.”

“Much effort and funding has been wasted on curcumin research,” says Gunda Georg, co-editor-in-chief of the *Journal of Medicinal Chemistry*, which published the review. Even so, she says, her journal sees a regular stream of curcumin manuscripts. Curcumin has been proposed to treat such disorders as erectile dysfunction, hirsutism, baldness, cancer and Alzheimer’s disease, says Guido Pauli, a natural-product researcher at the University of Illinois at Chicago and a co-author of the review. But it’s never yielded a proven treatment.

Pauli thinks part of the problem is that researchers don’t always know what molecule they are studying. Turmeric extracts contain dozens of compounds besides curcumin, which is itself used as a shorthand for three closely related molecules. In some cases, researchers may observe promising biological effects but ascribe activity to the wrong molecule.

Misinterpretations feed on themselves, Walters says. Curcumin gets reported as having an effect even if the assay was flawed. “People accept what is in the literature as being correct and then build a hypothesis, even though it doesn’t hold up.” And scientists don’t seem to check the literature to see whether compounds have been flagged as problematic. At least 15 articles on curcumin have been retracted since 2009 and dozens more corrected.

Many researchers are still optimistic about curcumin. “There is evidence that the biological activity of curcuminoids is real,” says Julie Ryan, a radiation oncologist at the University of Rochester Medical Center in New York. She says that it interacts with many different proteins and so works differently from many drugs. Ryan has tested curcumin in clinical trials for dermatitis on more than 600 people. Although she found no significant effect, she says there were trends that warrant further study. She thinks that chemically modified forms of curcumin might prove more effective at reaching tissues.

But the review shows that getting real answers will be tough, says Bill Zuercher, a chemical biologist at the University of North Carolina at Chapel Hill. “It may very well be the case that curcumin or turmeric extracts do have beneficial effects, but getting to the bottom of that is complex and might be impossible,” he says. ■



Beaver reintroduction is an example of a programme that could blossom after Brexit.

ENVIRONMENT

Brexit is chance for greener nation

UK environmental scientists plan to push for policy changes but are nervous about losing current protections.

BY DANIEL CRESSEY

Britain’s environment faces significant risks from Brexit, with protections for wildlife and millions of euros in funding for environmental programmes now facing an uncertain future. But the pending departure of the United Kingdom from the European Union will free lawmakers to craft UK-specific legislation — and some environmental researchers spot a rare chance to use their expertise to shape future policy.

“The decision to leave the European Union presents substantial risks, but also significant opportunities,” says Sue Hartley, an ecologist at the University of York, UK, and president of the British Ecological Society. She gave evidence to a parliamentary inquiry into the impact of Brexit on the environment, which was led by Member of Parliament Mary Creagh and released its conclusions on 4 January.

The process of leaving the EU is due to start by the end of March 2017, and must be completed within two years. To avoid a sudden change in how things work, the UK government says it will introduce a ‘great repeal bill’ that will largely convert EU laws into UK ones. But it will then be able to modify or strike out

EU laws, something that currently requires unwieldy negotiations with the rest of the EU.

Some environmental campaigners are worried about what this will mean for the EU legislation that currently safeguards UK birds and habitats. “The evidence has shown that these directives are effective,” says Martin Harper, conservation director of the Royal Society for the Protection of Birds. Creagh’s committee has called for an act to safeguard existing protections for UK wildlife ahead of the implementation of the great repeal bill.

But environmental researchers, many of whom have spent years pushing for reforms to huge EU programmes only to be frustrated by the slow pace of change, also spy an opportunity — in particular when it comes to one of the most contentious pieces of EU legislation, the Common Agricultural Policy, or CAP.

In the United Kingdom, most CAP funding is spent on direct payments to farmers to support their income. This amounts to around £1.8 billion (US\$2.2 billion) annually. A smaller proportion — £400 million — goes to programmes that benefit the environment, such as paying for buffer strips between fields to promote wildlife habitat or to reduce damage from fertilizers. ▶

▶ But scientists argue that more of the CAP money should go towards environmental protection. Reforms in 2013 were meant to make CAP greener, such as a rule requiring farmers to grow at least three crops to maintain biodiversity, but this did not assuage all concerns. “It’s pretty hard to make the Common Agricultural Policy worse than it currently is,” says Dieter Helm, an economist at the University of Oxford.

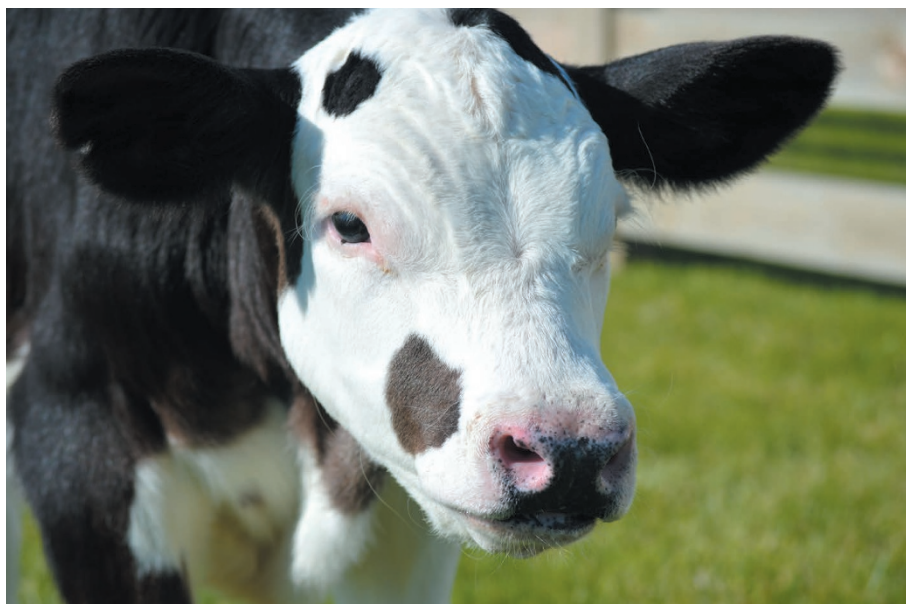
In September, Helm wrote a report exploring ways in which a post-Brexit United Kingdom might replace CAP (go.nature.com/2jksoc). His preferred option is a radical overhaul that would eliminate automatic subsidies to farmers. Instead, the government could target investment at rural programmes that provide proven benefits, such as reducing pollution or increasing biodiversity, he suggests. These could involve payments to farmers who modify their farms to provide such green benefits.

Richard Brazier, who studies the environmental impact of land use and agriculture at the University of Exeter and was a witness in the parliamentary inquiry, also spots an opportunity to reform CAP. His specialism is landscape restoration, in which farmed land is altered to provide better ‘ecosystem services’ alongside food production. One example is reintroducing beavers to benefit flood management. A UK-specific agriculture policy could aim to rewild between 1% and 10% of farmed land, he suggests.

He recommends that any new policy removes existing barriers to rewilding, such as CAP rules that effectively penalize farmers for transforming woodland or ponds into wildlife habitat that does not produce crops. The parliamentary report also mentions the possibility that rewilding, and the removal of these disincentives, could feature more prominently in UK-only laws.

But there are risks associated with losing CAP. The government has guaranteed to fund existing CAP payments until 2020, but on 4 January, environment minister Andrea Leadsom pledged to “design a domestic successor to CAP” while scrapping various pieces of EU legislation — including the three-crop rule — and “cutting the red tape that comes out of Brussels”.

Even researchers who have criticized CAP in the past fear that modifications could undermine its environmental benefits. Lynn Dicks, an applied ecologist at the University of East Anglia in Norwich, co-authored a highly cited critique of the 2013 reforms (G. Peèr *et al. Science* **344**, 1090–1092; 2014), but in 2013 she also reported that many schemes designed to protect wildlife produced consistent benefits (L. V. Dicks *et al. Conserv. Lett.* **7**, 119–125; 2014). “I think we’ve been quite innovative actually, within the CAP,” she says. “It’s terrifying to me that we might lose all of it.” ■



This hornless calf was created using gene-editing technology.

COURTESY OF RECOMBINETICS

POLICY

The issues facing Trump’s FDA chief

The next leader of the agency will have an opportunity to reshape its approach to regulation.

BY HEIDI LEDFORD

US president-elect Donald Trump wants to speed up drug approvals and broadly reduce government regulations. What that means for the US Food and Drug Administration (FDA) is not yet clear — but if Trump’s choices for other posts are any guide, he will look for an FDA commissioner to shake up the status quo.

The next FDA chief could shift the agency’s stance on everything from medical testing to clinics that claim to provide stem-cell therapies.

Until Trump announces his pick and that person is confirmed by the US Senate, the drug industry will struggle to map out its future, says David Fox, a partner at the law firm Hogan Lovells in Washington DC. “People in this industry need to plan substantially in advance,” he says.

Nature looks at what the next administration could push forward — or sweep away.

SWIFTER DRUG APPROVALS

The FDA has struggled to balance pressure for speedy drug approvals with its desire for convincing clinical data. The situation came

to a head in September 2016 when the agency approved a drug to treat Duchenne muscular dystrophy.

Patient advocates cheered eteplirsen, made by Sarepta Therapeutics in Cambridge, Massachusetts — one of only a few treatments for the devastating genetic disease. But some FDA reviewers were dismayed that the agency had acted on the basis of a clinical trial that included only 12 children and did not demonstrate changes in symptoms or disease progression.

Industry and patient advocates have been left to guess at what standards the FDA will apply to future decisions on drugs to treat rare diseases. “The new commissioner is going to face the aftermath of the Sarepta approval,” says Fox. “It’s a very big issue: his or her role is to help the agency manage the patient voice and maintain a certain standard.”

By law, the FDA must require “substantial evidence” of efficacy and safety before it approves a drug, but that term is subject to interpretation, says Fox. And the agency could soon come under tremendous pressure to lower the bar. One person thought to be under consideration to head the agency is investor Jim O’Neill of Mithril Capital Management in