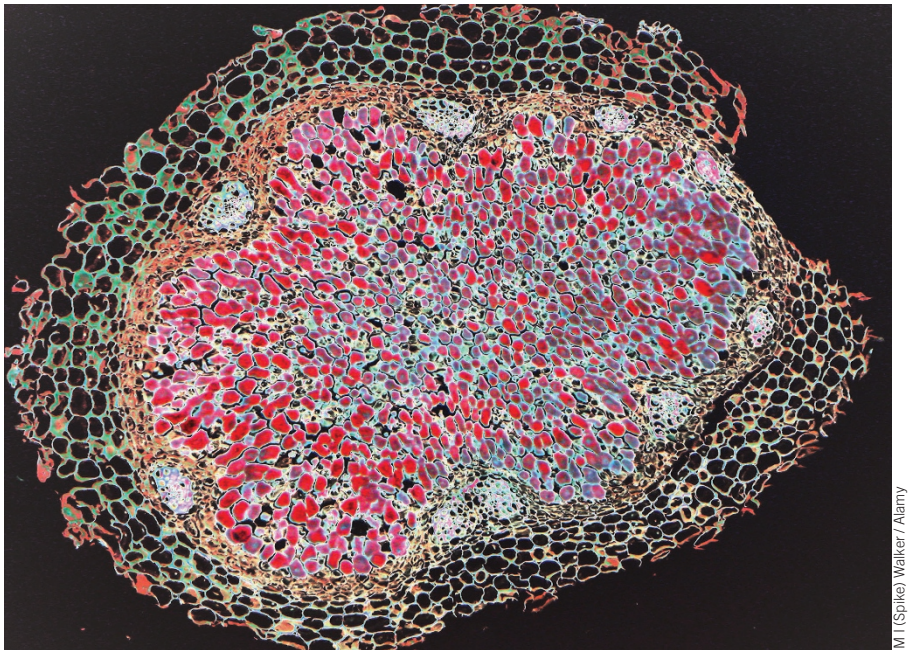
Patenting natural products just got harder

The US Patent and Trademark Office (USPTO) on March 4 issued new guidelines with far-reaching consequences for the biotech industry. Following publication of the *Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products*, it is now a lot harder than before for companies to patent natural products, such as antibiotics and therapeutically useful toxins, nucleic acids, peptides and proteins. "Many legal practitioners have raised a concern that the guidelines impose a new test for patent eligibility that is stricter than is required by law," says Kirsten Grüneberg, attorney at law and partner at Oblon Spivak in Alexandria, Virginia.

The new guidelines draw on two high-profile Supreme Court decisions: *The Association for Molecular Pathology versus Myriad*, which determined that isolated and purified DNA could not be patented (*Nat. Biotechnol.* **31,** 663–665, 2013) and *Mayo versus Prometheus*, which ruled that methods of determining optimal drug doses, based on levels of a naturally occurring metabolite were not patent eligible (*Nat. Biotechnol.* **30,** 373–374, 2012).

In issuing the new guidance (http://www.uspto.gov/patents/announce/myriad-mayo.jsp), the patent office aims to provide clarification for its examiners in light of those rulings. The new requirement is for a patent claim to show a 'marked difference' from a known natural law, material or phenomenon. To illustrate this, the document provides examples of hypothetical patent applications—as a cancer-combating compound isolated from a tropical plant, bacteria with energy-generating plasmids, a method for DNA sequence amplification using specific primers and a diagnostic for neurodegenerative disease based on detecting misfolded protein, and whether or not certain claims directed to these inventions might be patent eligible. The guidance adds the caveat that there are "no bright line rules" to patent eligibility and includes factors that weigh in favor of or against patent eligibility, such as whether or not the invention is "markedly different" from naturally occurring products.

But the breadth of the new patent evaluation is worrying, as it oversteps the Supreme Court rulings. The changes will make it more difficult for patentees to show eligibility and could prove a bonus to those challenging the validity of patents. "[The guidelines] will have a much larger negative impact on the biotechnology and pharmaceutical fields than the Supreme Court contemplated in its recent *Myriad* and *Prometheus* decisions," says Courtenay Brinckerhoff, a partner at Foley & Lardner, Washington, DC. "Getting a patent that claims a natural product or



M I (Spike) Walker / Alamy

Rhizobium bacteria form a nodule in broad bean root. A 1948 decision rejecting the patentability of *Rhizobium* bacteria mixes for nitrogen fixing has made its way into the recent guidance.

IN brief

Better than breakthrough scheme snags

The UK will allow compassionate use of unlicensed drugs under a new program launched in April by the Medicines and Healthcare products Regulatory Agency. The Early Access to Medicines Scheme is similar to the US breakthrough therapy designation in that it is intended to help fast-track drugs for life-threatening or seriously debilitating diseases with no adequate treatment options. But the UK scheme goes one step further than its US counterpart, by allowing doctors to prescribe drugs still in phase 2 or 3 testing if the agency believes there is a positive benefit-risk balance. One major concern over this scheme is lack of funding. With no government support to provide drugs to patients in the National Health Service (NHS) for free, companies will have to make an upfront investment to participate. "Without centrally funded reimbursement the early access scheme risks being underutilized," says Steve Bates, CEO of the UK BioIndustry Association. A similar program exists in France, the cohort Authorized Temporary Use program. But the French government pays for compounds used in the program. The UK's scheme begins with companies submitting an application for a Promising Innovative Medicine designation. Once such a designation is obtained, products will be channeled through a new, collaborative appraisal by the National Institute of Health and Care Excellence (NICE) and a new commissioning scheme in the NHS. For small companies, manufacturing the novel drug and meeting demand may be problematic. Early access programs are also risky because a drug might be killed if it is not effective in seriously ill patients or causes serious side effects. But Bates points out that these schemes are aimed at drug developers already operating in challenging areas, such as rare diseases and gene therapy. "I wouldn't expect everyone to be interested." A few days before the UK scheme was announced, the European Medicines Agency launched a pilot project designed to give early approval to products still in development that address an unmet need in restricted patient groups. The principle behind this adaptive licensing pilot is that early phases of data gathering would eventually allow the license to be expanded to different categories of patients. "Adaptive licensing is part of the [early access scheme] mix," says Bates. "It goes with the grain of thinking that as you accumulate evidence you get a license to do more trials." *Nuala Moran, London*