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European Biotechnology

Life Sciences and Industry Magazine

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Interview

Olivier Litzka from Andera Partners on VC and how the biotech industry is working its way out of the trenches.

FREE EXCERPT

Targeted radiotherapy powered by Biotech

Clinical studies: CTIS
The new EU study portal is well-meant, but disappointing

CRISPR/Cas & Co.
Europe set to fail at setting up liberal rules for new breeds

Bioprocessing
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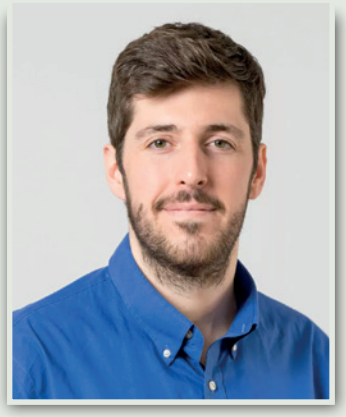
Cultivated meat debate clouded by misinformation



SETH ROBERTS, is a policy manager with the international nonprofit and think tank the Good Food Institute Europe, specialising in the regulation of food such as cultivated meat and precision fermentation. He has expertise in EU and national government food safety policy and works with public authorities, food safety experts and businesses to secure a clear and evidence-based regulatory path to market for alternative proteins. He brings experience from the UK Civil Service and the House of Commons.

As cultivated meat moves closer to commercialisation, we are seeing a worrying trend of misinformation entering the public debate. This food can play a vital role in ensuring Europe's food system is fit for the future – helping satisfy the growing demand for meat while boosting food security – but political opposition has mounted, with the Italian government taking the controversial step of banning cultivated meat.

Many of the false claims dominating the debate leading to this ban were repeated in an item of 'any other business' brought to a recent meeting of the EU's 27 agriculture ministers. This included references to a preprint UC Davis study claiming cultivated meat would have a larger carbon footprint than beef – highlighted by a Changing Markets Foundation report as having been used as part of a misinformation campaign.

As well as not being peer-reviewed, this study is based on the incorrect assumption that the commercial production of cultivated meat would rely on pharmaceutical-grade cell culture media. This doesn't reflect current practices, and peer-reviewed data has shown that food-grade ingredients can support cell growth. The findings deviate significantly from the wider literature, including a peer-reviewed study, based on input from cultivated meat companies and media suppliers, showing that producing cultivated meat at scale using renewable energy could lower climate emissions by 92% compared with conventional beef. The note also cited a 2019 University of Oxford study as evidence of cultivated meat having worse climate impacts than conventional meat. In fact, while this study was conducted when cultivated meat research was less developed and was based on a fossil fuel-intensive energy mix, it still found that cultivated meat is much better for our climate than the 'best' conventional meat production systems for at least the next 100 years.

Another claim is that cultivated meat does not provide higher animal welfare standards due to the use of foetal bovine serum (FBS). But while FBS is used as a medium in biotechnology settings, its price, inconsistency and limited supply means it cannot be used for producing cultivated meat at scale. Many companies have moved away from it and an FBS-free cultivated meat product has been approved in Singapore. It's vital that these debates are informed by evidence and aren't clouded by misinformation. For those looking for it, there is a wealth of independent information such as FAO & WHO and UNEP reports providing details about cultivated meat's safety profile and environmental benefits.

The field has moved on a lot since it was developed by Dutch scientist Dr Mark Post just over a decade ago but remains in its infancy. The EU is home to some of the world's best scientists in this area, but they need certainty from policymakers if their innovations are to benefit Europe rather than being used overseas. ■

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COVER STORY

Targeting cancer with Radio-Biotech

Radiopharmaceuticals have turned into a hot commodity when it comes to M&A financing and deals. Targeted therapies that employ high-energy attachments linked to antibodies, small molecules or peptides promise fewer side effects and a localised attack on the tumour. Novartis initially cracked open the door with an innovation from France. Now investors are trying to play catch-up, and startups have seen a surge in demand. The companies involved are both toolmakers and those digging for radioactive gold.

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CLINICAL STUDIES

Critics on CTIS

Even before its launch last year, drug developers, CROs, ethics committees and clinicians began criticising the technical implementation of the EU study portal CTIS. Though the most serious programming errors have now been eliminated by the EMA, the goal of simplifying the registration of multi-centre trials and making the bloc more attractive to trial sponsors was clearly missed.


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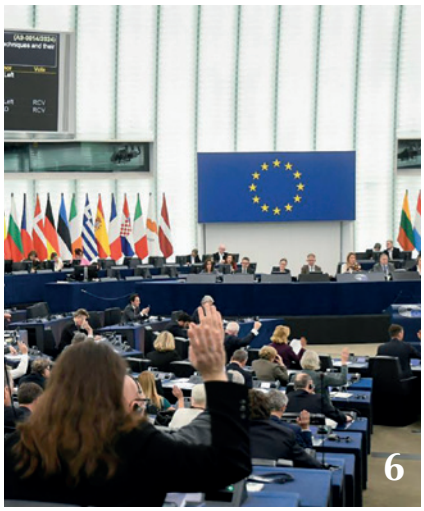
NGT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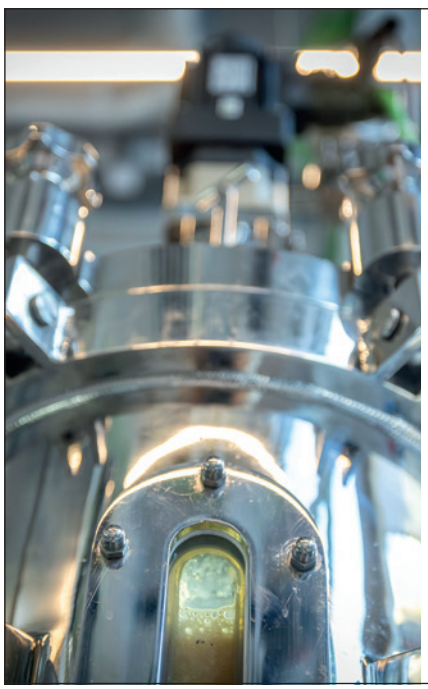
NGTs: No smart rules?

Although the European Parliament has voted in favour of the EC's draft regulation putting 94% of plants bred using new genomic techniques (NGTs) on an equal footing with conventional plants, EU ministers are unable to come to an agreement. This means that the law is in danger of failing.



SPECIAL

Bioprocessing

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EDITORIAL

Climate alarm

Anyone who has seen the film 'The Day After Tomorrow' won't be thrilled by the climate modelling published recently by Dutch researchers. They predict a drop in temperature of 2°-3° Celsius per decade by the end of this century in the northern hemisphere due to a predicted collapse of the North Atlantic Current (AMOC) as a result of global warming and resulting disruption to how seawater of different salinities mixes. While the northern hemisphere is cooling, says the model, the southern hemisphere will grow hotter and hotter – with presumably devastating weather extremes similar to those in the film.

The scientific alarm is an urgent reminder of the need for action. The time for politically motivated, industry-friendly climate cosmetics must come to an end. This means finally investing massively in climate-friendly biotechnologies, as the US has done with its bioeconomy strategy focussing on the potential of synthetic biology. The still baffled, Brexiteered UK wants to follow suit with the announcement of £2bn over 10 years.

The plans focus on biotech in medicine, food production and the breeding of climate-adapted plant varieties. The EU, on the other hand, is currently failing to adapt the authorisation of new genomic techniques, the acceleration of clinical trials and photosynthetically produced biodiesel. What has to happen to finally force change?

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Thomas Gabrielczyk
Editor-in-Chief

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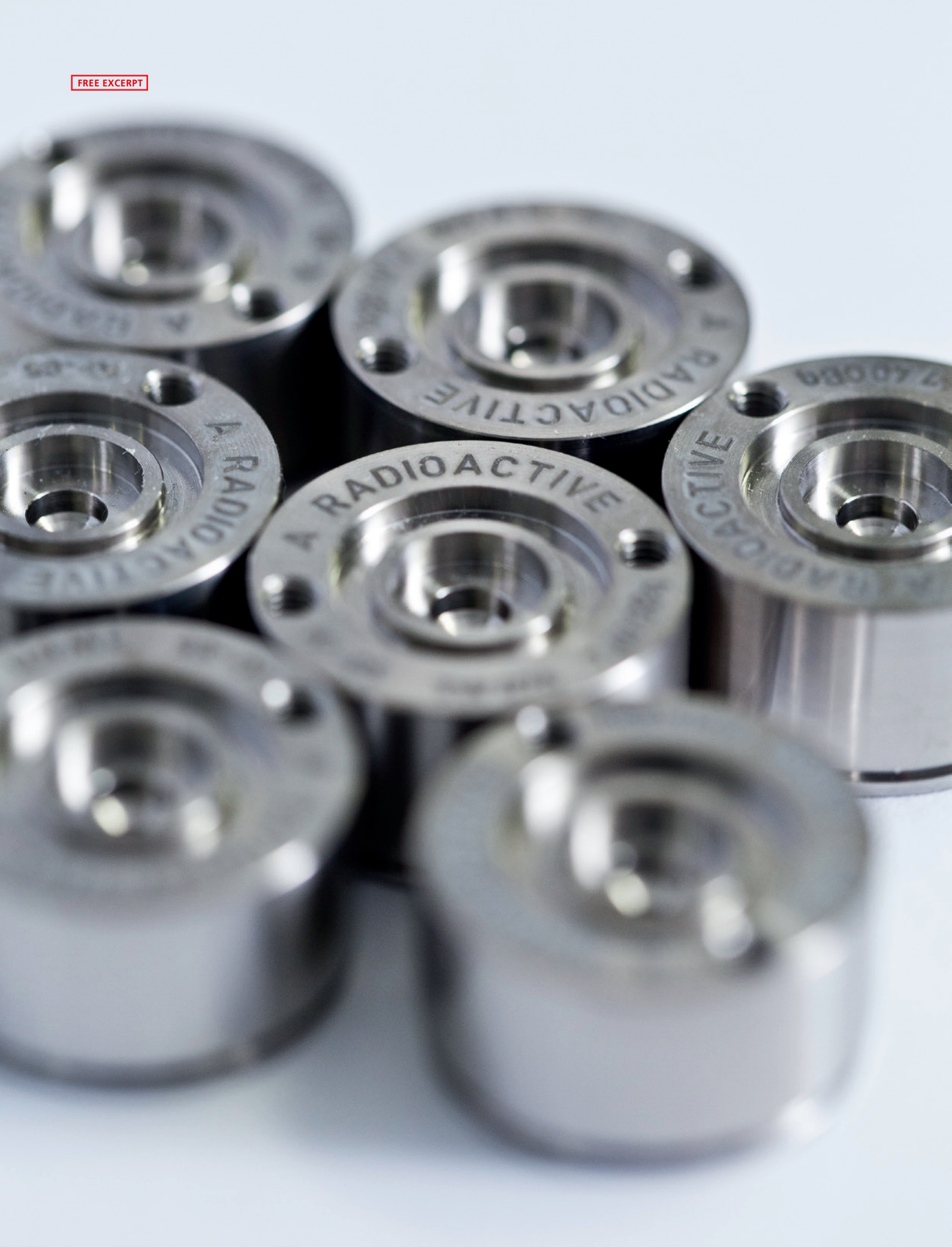

Targeting cancer with Radio-Biotech

ONCOLOGY Steel, rays, poison ... those are the traditional medical approaches to treating cancer. Surgery, radiology and chemotherapy – or a combination thereof – have been the weapons of choice for oncologists for decades. Targeted radiotherapy is a newer molecular variant designed to maximise damage to the tumour and minimise damage to surrounding tissue. Now the success of approved radiopharmaceuticals has caught the attention of investors and Big Pharma.

The big idea behind radiopharmaceuticals is to combine the strengths of two kinds of cancer treatments – radiology and targeted therapies. In simple terms, it involves attaching radioactive isotopes to a molecule, then irradiating cancer cells with a high degree of specificity and selectivity by matching those molecules to known targets.

Funding is piling up

Headlines about deals in the pharma industry make it clear that global interest in radiopharmaceuticals is growing, and some major deals in the area stand out. The value of the global radiopharmaceutical industry was estimated at around US$5bn in 2017, and could grow to US$15bn in the coming years in the United States alone, according to industry experts.

Investments in the sector are correspondingly large. Novartis AG alone has spent around US$6bn on acquisitions, and is currently regarded as the global leader in the field. The Swiss multinational entered it in 2017/2018 with its US$3.9bn purchase of French company Advanced Accelerator Applications SA and its then-hopeful Lutathera, which addresses gastroenteropancreatic neuroendocrine tumours (GEP-NETs). With its approval in 2018, Lutathera became a major role model in the radio space, and has since been viewed as a door-opener. Later in 2018 Novartis spent a further US$2.1bn to acquire Endocyte Inc., integrating Pluvicto (177Lu-PSMA-617), which uses lutetium (^{177}Lu) – a beta-emitter targeting prostate-specific membrane antigen (PSMA). It received approval in 2022.

Although the pandemic posed major challenges, more deals followed soon. In June 2021, Bayer AG acquired Noria Therapeutics Inc. and PSMA Therapeutics Inc. The aim was to develop a prostate cancer treatment that uses a small molecule to deliver radioactive therapy to cells carrying PSMA markers. However, little has been heard to date about this me-too prostate product. Last year Eli Lilly also acquired Point Biopharma Global for US$ 1.4bn after a small bidding war for the two therapeutic programmes. They target metastatic castration-resistant prostate cancer and also GEP-NETs – other me-toos – but the deal included production facilities as a sweetener.

RayzeBio has also recently made headlines. Founded in California (US) in 2020, the company raised around US$418m in four venture capital rounds before going public on the NASDAQ last September with a gigantic IPO totalling US$311m. Its lead therapeutic candidate uses the same molecule as Novartis' Lutathera to also target GEP-NETs, but swaps out lutetium-177 for actinium-225 – an isotope that emits more destructive alpha particles. It's capable of delivering hundreds of times the energy in a much smaller radius, one only a few cells in depth. Just three months later, in December 2023, Bristol Myers Squibb acquired RayzeBio for US$4.1bn, topping off a massive buying spree. In just a few months in the second half of 2023, BMS spent around US$24bn on business development and acquisitions.

Narrow focus on targets

These examples show that the focus of development was essentially on prostate cancer and special forms of neuroendocrine tumours. Similarly, the target molecules are limited to two main focuses of interest: PSMA and somatostatin receptor 2 (SSTR2), which are overexpressed in GEP-NETs and extensive-stage small-cell lung cancer (ES-SCLC). New targets like Fibroblast Activation Protein (FAP) are also slowly getting some limelight, however, as indicated by an in-licensing deal of two FAP-targeting peptides from German biotech company

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Well-intentioned, badly done: The digital EU reporting system for clinical trials CTIS, managed by the EMA, allows a reporting EU Member State to register a multi-centre trial in any number of EU Member States at the same time with a single notification. The idea is to achieve better coordination through better communication. Trials registered under the old EudraCT system must be switched to CTIS by 31 January (2025) at the latest.

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CTIS: Clinical trials in slowdown

INFORMATION SYSTEMS Even before its launch last year, drug developers, CROs, ethics committees and clinicians began criticising the technical implementation of the EU study portal CTIS. Though the most serious programming errors have now been eliminated by the EU authority EMA, the goal of simplifying the registration of multi-centre trials and making the bloc more attractive to trial sponsors was clearly missed. What are the consequences for Europe?

Clinical trials that are carried out in a timely, compliant and successful manner can shorten time to market, and thus significantly increase sales of drugs within patent terms. It's therefore no surprise that study sponsors look for locations that are able that help get their medical innovations to patients as quickly as possible. Competition between potential sites fuels the global race to market, so it boils down to hard cash. According to Markets & Markets, the global clinical trials market size stood at US$54.24bn in 2022, and is projected to grow by 6.9% annually to US$92.45bn by 2030.

In order to improve the position of the EU against rising star China and the undisputed top dog – the US – in terms of studies carried out (see Fig. 1, p. 56), the European Commission developed the idea for a digital portal back in 2012 as part of EU Regulation 536/2014.

"The idea behind the adoption of EU Regulation 536/2014 was a good one," stresses Martin Krauss, Managing Director of FGK Clinical Research GmbH and Chairman of the Board of BVMA e.V., which represents the interests of Germany's contract research organisations (CROs). "The digital, simultaneous application for the European Economic Area EEA (30 countries) was meant to harmonise the previously time-consuming sequential application for clinical trials, and enable the start of trials with an identical protocol in each participating country at the same time," he explains, "which is particularly important for large multi-centre pivotal trials."

> To put it mildly, the fact that CTIS is not working so well makes Europe unattractive to study sponsors – we have to realise that.
>
> Biopharma stakeholder, confidentially

Accordingly, Article 80 of the law states: "The portal must be kept up-to-date with the latest technology so that no unnecessary workload is created." On paper at least, the concept sounded convincing. Application via CTIS would be sufficient for all participating countries, and significantly speed up recruitment. In reality though, even after a 12 month technical check before the new system became mandatory – with a two-year transition period for ongoing studies registered under the old EudraCT system – it didn't work right. Files couldn't be uploaded, as well as data on members of the ethics committee. The maximum data volume for the documents required in the application was also too small, among other issues. As the response deadlines for enquiries to the applicant were often tight and fixed to the minute, costly new applications had to be submitted if initial uploads to the portal were unsuccessful.

Well-meant, but disappointing

So even before CTIS went into effect on 31 January 2023, critique about the new EU study portal had grown loud. "It's sad but true that, according to experts, it wasn't state-of-the-art when it was launched," according to Dr Thorsten Ruppert, Senior Manager Research, Development, Innovation from German pharmaceutical association vfa. He told European Biotechnology that "the implementation of the good idea is disastrous" – an assertion stressed by associations and chief investigators.

In the months since the launch, the European Medicine Agency (EMA), which administers CTIS and is responsible for its maintenance, has made a huge effort to rectify the most serious errors. No easy task on a project patched together by three tenders over nine years. However, completing applications in the system is still very time-

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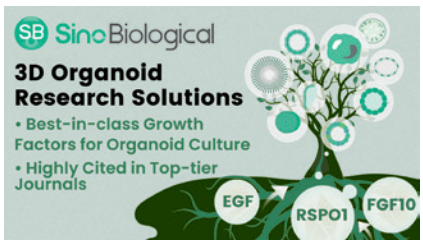
Organoid research



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