



European Biotechnology

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Interview

Frédéric Pâques,
CEO of Standing
Ovation SA, on
why vegan cheese
made with microbial
casein can help save
the climate.



FREE EXCERPT

Biotech Financing

Crisis? What Crisis?

INDUSTRIA BIOTEC

Biotech solutions are ready –
time to change the paradigm

Focus Pharma Services

Record pandemic-powered profits
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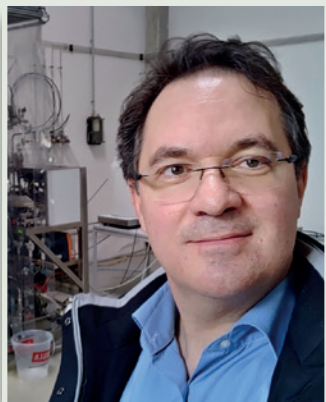
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Why we need the switch from oil to biotech now



DR ALEXANDER KRAJETE is managing director of Krajete GmbH, a company that pioneers high-performance gas fermentation and gas purification. He holds a PhD in chemistry with postdoctoral experience from UC Berkeley. Alexander started his career in the petrochemical industry with Borealis Norway in 2004, where he was project manager for polyolefin upscaling and senior scientist for hydrocarbons. Inspired by archaea, he founded Krajete GmbH in 2012.

Our species – modern humans, or homo sapiens sapiens – has ever striven for progress. And progress was greatly enabled by fire, a fundamental chemical phenomenon that allows the fast release of large amounts of energy. In the modern age, industry began tapping into coal, oil and more recently shale gas as ‘feedstocks’ (known in biology as ‘substrates’), using heat from their fire, and high pressure, to crack substances to yield yet other fuels and base chemicals. Those industries use ‘prefermented’ compounds as an energy source. But processing conditions are harsh, while side-products are often unknown and, in many cases at least, toxic. The exploitation of fossil resources allowed economic growth during an era when by-products and the long-term effects on our species and the environment were secondary worries. Those days are over.

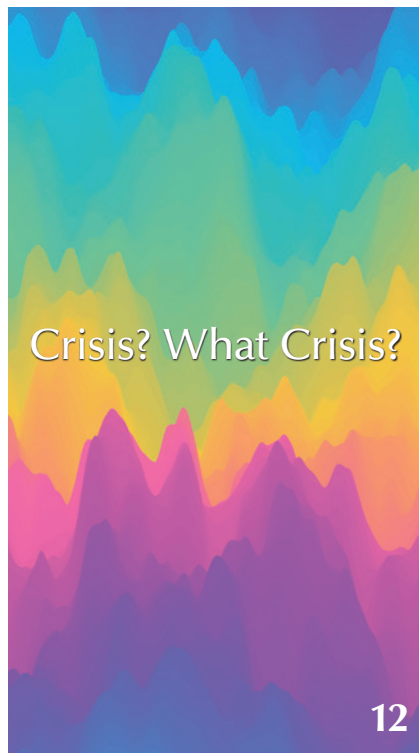
So why does biotechnology provide long-term solutions to the legacy of past economic growth? Why has it been so long ignored? Why has it taken so long for large corporations to discover the charms of enzymes and microbes, and has it really? Or do they just want to keep running their old profitable plants under the guise of green promises or because they lack the know-how?

Unlike chemistry that requires other catalysts, biotech employs enzymes and microbes to accomplish the transformation from component A to B. The biggest difference between the two is intimately related to energy and selectivity. Biotech processes are ‘mild’. They occur within the boundaries of life. And due to the nature of the factors that drive them, enzymatic processes are also selective, influencing for instance the amount of desired product produced. Biotech processes additionally arise from evolved systems, and both products and ‘waste’ are compatible with Nature. Conventional industrial chemical processes, in comparison, are harsh, often involving high temperatures and high pressures, yielding byproducts and waste that is not compatible with Nature. In the balance that must be struck between a) energy demand, b) selectivity and c) overall fit with Nature, only biotechnology offers ways to exploit resources in truly long-term and sustainable ways.

But because our societies have been powered by fossil fuels for centuries, it’s difficult for decisionmakers to understand and execute new frameworks in the modern world. It is therefore of utmost importance to look holistically at the big perspective, and question economic growth as the sole key measure for ‘progress’. We need a perspective that equally values a long-term fit with the environment. The impact of a biotech-based economy would quickly become clear (in the form of a restored global ecosystem) if measures are taken now to move towards a fast ‘Global Fossil Exit’. Humanity needs to rediscover the circularity common to ancient cultures and center it again as a fundamental pillar of modern cultures. We can no longer afford to simply ignore our central ally and partner – Nature – in favour of short-sighted economic gains. ■

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COVER STORY



M&A – hints of a looming crisis?

2022 looks set to be the worst year for biotech Mergers & Acquisitions since 2018, and some experts have speculated it might herald the start of a new crisis for the sector. External financing is indispensable for drug developers. In the absence of external capital, achieving growth turns into an even greater struggle, and innovation slows. We take a deeper look into the causes behind the 'new normal' in partnerships and licensing, and break down why a predicted M&A wave is not cresting as quickly as expected.

INSIGHT EUROPE

- 6 AMR: Big Pharma's TEE initiative
- 8 Banks and policymakers driving climate change
- 10 Agri-coalition for genome editing
- 11 EU rules on biogas production

ECONOMY

- 20 Analyst commentary
- 21 European Biotech Stocks
- 24 Innate immunity and its power in cancer therapy
- 26 Interview: Frédéric Pâques, CEO, Standing Ovation SA
- 28 Clinical trials
- 30 Focus Pharma Services: CDMO/CRO business set to grow
- 34 Cell factories: the heart of rAAV manufacturing
- 36 Blow-Fill-Seal technology and vaccine delivery
- 38 Interview: Christian Nafe, CFO, leon-nanodrugs GmbH

- 40 Lessons learned in the face of new health challenges
- 42 AGC Biologics doubles mammalian capacity
- 44 Wholistic approach to strategic consulting

REGIONAL NEWS

- 65 Special Industrial Biotech Cluster: Toulouse White Biotechnology
- 70 Northern Europe: Sweden, Denmark, Norway, Iceland and Finland
- 72 Western Europe: France, Belgium, The Netherlands and the UK
- 74 Central Europe: Germany, Switzerland and Austria
- 76 Southern Europe: Italy, Spain, Croatia and Portugal
- 78 Eastern Europe: Czech Republic

SCIENCE & TECHNOLOGY

- 79 At the interface of AI, healthcare and data science
- 80 Biofilms for production
- 81 AI-enabling predictive diagnostics; Bio-based electronic devices
- 82 Ultra-low freezers: Stability of cancer biomarkers

PICK & MIX

- 46 Biopeople
- 83 News from Biotech Austria, the ECBF, YEBN and the SBA
- 88 Company index/ New product
- 89 Events
- 90 Encore

INDUSTRIAL BIOTECH

(Bio)economy 2.0

For years, policies promoting industrial production modelled on naturally-occurring cycles have been little more than a thin green veneer used by oil and chemistry multinationals. At the new forum INDUSTRIA BIOTEC, companies presented both new ideas and long-ignored solutions that – in cooperation with politics – could help avert the looming gas and climate catastrophes.



FOCUS: PHARMA SERVICES



Determined to grow

Over 40,000 on-site visitors to the CPHI in Frankfurt have shown that the COVID-19 pandemic has had a positive impact on the (bio)-pharmaceutical sector. A new CPHI annual survey predicts how business will develop in the future, with prospects for CDMOs and CROs looking rosy.

EDITORIAL

Empty promises?

When politicians talk about climate change and the associated systemic shift from nature-exploiting to nature-conserving processes, they often sound reasonable and responsible. This was also the case at COP27 in Sharm-el-Sheikh in Egypt. But the ‘error’ in the massively underestimated national CO₂ emission budgets of the G20 countries – revealed by ex-US Vice President Al Gore’s Climate TRACE coalition – was not taken as an opportunity to decide immediately for binding production budgets. Nor was a decision made to shut down CO₂ emitters, which can now be identified by satellite, to make up for lost time in decarbonising the atmosphere (see p. 8). Instead, the somewhat pointless promise was made that from now on, we would take an annual look at the depressing CO₂ figures. In view of how little time is left to deflect the consequences of climate change and lower the world’s still excessive energy consumption, we could use another Al Gore to help push next-gen biotechnological processes for environmental and climate protection (see p. 58). Significant investments are needed to scale-up nature-compatible production processes and realise the biologisation of industries. At the premiere of the INDUSTRIA BIOTEC conference, experts explored rational, lobby-free ways out of the climate and energy crisis – that didn’t rely on empty promises.



Thomas Gabrielczyk
Editor-in-Chief

SPECIAL

Biofairs Compass

- 48 PharmaPack Europe, Paris, France
- 50 AMR Conference, Basel, Switzerland
- 52 BIO-Europe Spring 2023, Basel, Switzerland
- 54 Swiss Biotech Day 2023, Basel, Switzerland
- 56 Connect in Pharma 2023, Geneva, Switzerland





Full house at BIO-Europe 2022 in Leipzig

Crisis? What Crisis?

FINANCING External financing has proven indispensable for small biotech companies in the drug arena, with the majority of firms viewing it as essential for accelerated development. Where external capital is lacking, growth becomes more difficult, and innovation slows. The ‘new normal’ involves partnerships and licensing, especially in Europe, while the M&A wave is not building as fast as once predicted.

Few companies expect to be worse off in 2022 than they were before the pandemic. Fast, generous political aid and a strong recovery in demand in the first half of this year should help prevent it. Overall, 84% of companies expect sales to at least return to pre-pandemic levels in 2022. That’s the survey result across all sectors that emerged from the European Investment Bank’s (EIB) investment survey at the beginning of November. On the flip side, opinions about the future sounded less positive: the Ukraine war and its consequences look set to “test the resilience of companies considerably”. Investment conditions have also deteriorated significantly, hamstrung by the energy crisis, uncertainty and slowing global growth. Expectations regarding the economic situation slipped again into the red (from +27% to -53%). There was also a turnaround in the assessment of the business outlook (down from +34% to +3%), as well as in the outlook for the political and regulatory climate (-40%) and access to external finance (-8%).

View of biotech/pharma

With this dim view of the future from across industries, pharmaceuticals/biotechnology probably shouldn’t have high hopes, right? But depending on the interlocutor, the entrepreneurial perspective or the level of development of the company or its products, you hear very different sounds from the community. “On paper, the record cash reserves of the big

pharmaceutical companies, the steep, rapidly approaching patent cliff and the low public biotech valuations should lead to a buying frenzy,” wrote Melanie Senior in a recent commentary in *NATURE BIOTECHNOLOGY* (*Nature Biotechnology* Volume 40, 2022). And since stock markets within biotech indices are still falling, biotech companies short of cash were hopeful the pharma industry would buy up the external innovation on offer a little more indiscriminately, Senior added.

But that’s not happening. Many predicted a new surge based on a wave of top valuations and stock market prices piling up during the pandemic, foreseeing a buying wave in mergers & acquisitions (M&A). It has not failed to materialise completely, but hasn’t turned into the hoped-for spring tide – at least so far. Pfizer’s US\$11.6bn acquisition of

Biohaven Pharmaceuticals in May was a high point in 2022. But a possible mega-deal (rumoured to be worth around US\$40bn) between Merck and Seagen remains stuck, whether for substantive reasons, because of differences over the valuation, or that they’re simply shying away from striking such a major deal in times like these – maybe a combination of all of the above. Outwardly, both parties continue to claim that there are just some details left to be cleared up. However, without it, at the current pace, 2022 is set to be the worst year for M&A since 2018.

By the end of August, the total value of acquisitions in 2022 was just half that of 2021, which in turn was low compared to 2020 and 2019 (Fig. 1). Accord-

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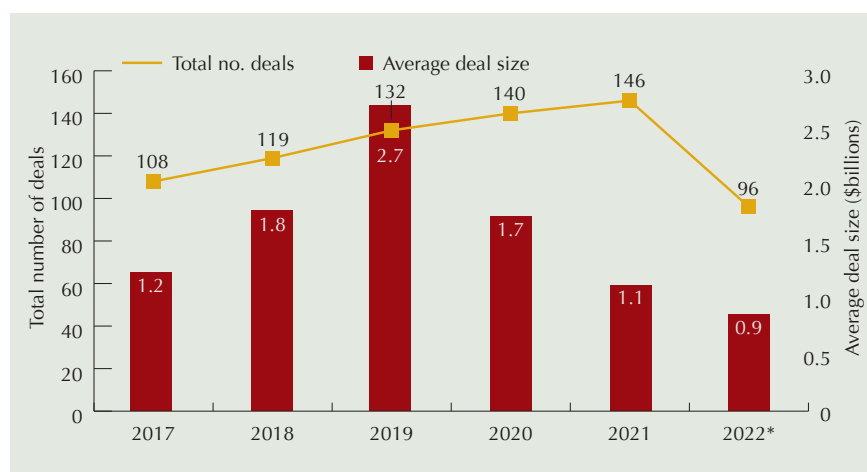


Fig. 1: M&A over a five year period. The average size of deals has fallen. *Through August. (Source: BioCentury BCIQ in *Nat Biotechnol* 40, 1546–1550, 2022)



This year's **INDUSTRIA BIOTEC** took place in a former brewery: the **KINDL** Centre for Contemporary Art in Berlin. The spirit and topics are featured in a short film, which is available online. Just scan the barcode and watch. More information about this event – organised by **BIOCOM AG** – can be found here: [→ https://industria-biotec.com](https://industria-biotec.com)

White Biotech: New kids on the block

INDUSTRIA BIOTEC For years, policies promoting industrial production modelled on naturally occurring cycles that don't exploit natural resources but re-produce from waste have been little more than a green veneer used by oil and chemistry multinationals. At the new forum INDUSTRIA BIOTEC, companies presented both fresh and long-ignored solutions for averting the looming gas and climate catastrophes in cooperation with politics, while experts took a close, hard look at the lobbies involved.

Conceived as a showcase for modern industrial biotechnology solutions for the energy and climate crisis, the premiere of INDUSTRIA BIOTEC in Berlin turned out to be unexpectedly political. While the EU High-Level Bioeconomy Conference 2022 running in parallel in Brussels favoured agricultural and forestry bio-based solutions as an alternative to petrochemicals, the biotech entrepreneurs and engineers in Berlin presented innovative microbial and cell biological solutions that have received less political attention so far. These promise an additional massive reduction of CO₂ emissions, which are currently rising at an annual rate of 0.65% (from 11/2021 to 11/2022). In Berlin, biotech innovators made clear how surprisingly much they can contribute to solving the energy and climate problems. They emphasised the importance of immediate political support to replace nature-destroying petrochemical production with sustainable production as quickly as possible.

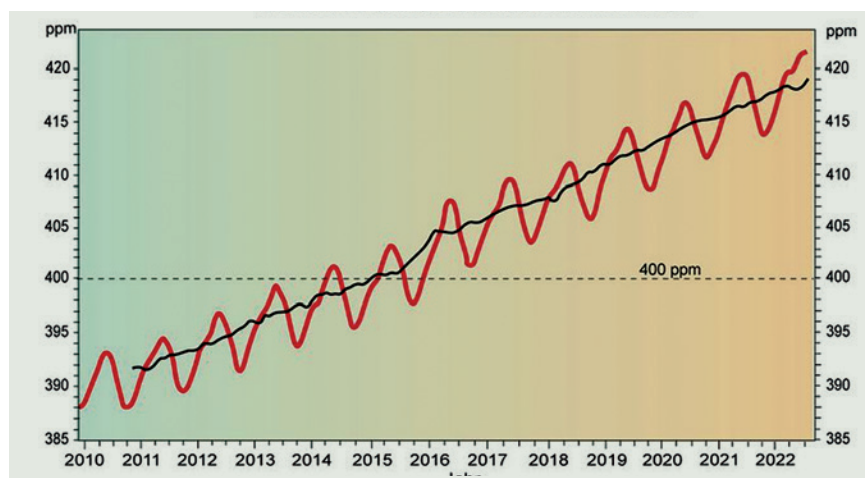
Industrial biotech – a driver

“We already have the technologies that will make it possible to bring atmospheric CO₂ levels down to 1990 levels”, said Aneri Pradhan, COO of sustainable energy-focused, \$1.5bn non-commercial biotech

accelerator New Energy Nexus (Thailand). “But we finally need the support of the public sector and politics for this. Firstly, to be able to scale-up fermentation plants. Secondly, to encourage consumers to consume more sustainably.” This astonishingly optimistic outlook on solving the climate and energy crisis was not unique at the first INDUSTRIA BIOTEC at the beginning of October. At the event, biotech experts of various stripes from all over Europe were in unanimous agreement that the petrochemical era must be brought to

an end as soon as possible, and the billions in subsidies that support it should instead quickly be pivoted to create publicly funded upscaling centres for energy- and space-saving microbial conversion and recycling processes (see report on COP27, p. 8). In general, experts at the conference agreed that the greatest potential for CO₂ savings lies in a new energy mix that includes biotech alternatives to oil, gas and coal burning for energy generation and

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Atmospheric carbon dioxide concentration has risen from 278ppm in the pre-industrial era to currently 417.95 ppm (November, 2022) as measured at the Mauna Loa observatory in Hawaii. Since 1990, when CO₂ emissions hit 353ppm, levels classified as a climate threat have only grown. Growth is currently around 0.65% yearly.

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SentinusAI™ is a powerful and self-evolving protein design engine created by Ainnocence. Its database contains up to 100 million human antibody sequences as well as an extensive collection of human/animal viral antigen information, resulting in high-confidence prediction of binding affinity. Antibody affinity maturation is a popular module of SentinusAI. Its close-loop nature guarantees that the model creates better antibodies by learning from each cycle of the experimental results. It has since delivered affinity-matured antibody sequences with an average hit rate of 15% and successfully increased affinity by three orders of magnitude. ■

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AbbVie Inc. (USA)	14
Abivax AB (F)	20
Affimed (DE)	24, 28
Affinivax (USA)	14
Afyren (F)	68
AGC Biologics (USA)	42, 46
Akribion Genomics (DE)	60
Alnylam Pharmaceuticals Inc. (USA)	16
Ambrosia Bio (IL)	65, 68
Anjarium Biosciences AG (CH)	46
APIM Therapeutics AS (NO)	71
Apollo Health Ventures (USA)	75
Arvinas Inc. (USA)	73
Asabys Partners (ES)	77
AstraZeneca (GB/SE)	18, 28
Avrobio Inc. (USA)	70
B Medical Systems S.a r.l. (LU)	7, 82
Badische Peptide & Proteine GmbH (DE)	60
BASF (DE)	63
BEAM Alliance / bamconn GmbH (DE)	50, 51
Bel Group (F)	60
BelleVue Asset Management AG (CH)	16
Better Nature (GB)	68
BioArctic Neuroscience AB (SE)	70
BIOCOM AG (DE)	58, 84
Biohaven Pharmaceuticals (USA)	13
BioMarin Europe Ltd. (UK)	16
BioNTech SE (DE)	20, 28
BioRN Cluster Management GmbH (DE)	25, 79
Biotals NV (BE)	72
BIOVIAN Ltd (FI)	31, 34
Blue Horizon Corp. AG (CH)	64
Blue Whale Material LLC (USA)	64
Bone Therapeutics (BE)	72
Brain Biotech AG (DE)	60
Bristol-Myers Squibb (USA)	14, 28
Calecto Inc. (DK)	29
Carbios SAS (F)	10, 66
CellPoint BV (NL)	18
Cellugy (DK)	65
Charles River (USA)	6
Cultivated Biosciences (CH)	65
CZ Vaccines (Zendal Group) (ES)	35, 40
Dionymer (F)	68
Easyfairs Group, Connect in Pharma (BE)	56, 57
EBD Group (USA)	54, 55
ECBF Management GmbH (DE)	69, 87
Eeden GmbH (DE)	10
Elaia (F)	68
Emscher Genossenschaft/Lippeverband (DE)	64
Enhanc3D Genomics Ltd. (GB)	73
EpiEndo Pharmaceuticals (IS)	71
Eppendorf Austria GmbH	CP4
Esencia Foods (ES)	60
European Biotechnology Network (B)	23
Evgen Pharma (UK)	73
Evonik Industries AG (DE)	64
FCF Corporate Finance GmbH (DE)	17
FGK Clinical Research GmbH (DE)	29
Forbion Capital Partners (NL)	16
Formo Bio GmbH (DE)	61
Galapagos NV (BE)	18
GlaxoSmithKline (UK)	6, 14, 28
Global Bioenergies SA (FR)	68
Heidelberg Pharma AG (DE)	29
Hookipa Biotech AG (AT)	75
Immunetep SA (PT)	76
Infarma Markets CPHI/Pharmapack (UK)	48, 49, CP3
Inpixon GmbH (DE)	11
ISA Pharmaceuticals B.V. (NL)	28
Johnson & Johnson (USA)	6
Krajete GmbH (AT)	3, 60, 62
L'Oréal (FR)	68
LABORATOIRE Unither (FR)	33, 36
leon-nanodrugs GmbH (DE)	38
Lesaffre (FR)	68
Limagrain Genetics SA (FR)	68
LISAvienna (AT)	19
LogicBio Therapeutics (USA)	18
LXP Group GmbH (DE)	63
Mablink Bioscience SA (FR)	73
Meatable BV (NL)	61
Medrara Therapeutics (DE)	74
Medsenic SA (FR)	72
Merck & Co. (USA)	13
Metabolic Explorer (FR)	68
Micropep (FR)	68
Mimetas BV (NL)	72
Minoryx Therapeutics S.L. (ES)	76
MorphoSys AG (DE)	74
MSD Sharp & Dohme (USA)	6
MyBIOS (AT)	65
Myllia Biotechnology (AT)	75
MyoPax ApS (DK)	70
Neuraxpharm Arzneimittel GmbH (DE)	76
NeuVasQ Biotechnologies (BE)	46
Nordic Nanovector AS (NO)	71
nova-Institut GmbH (DE)	63
Novo Nordisk A/S (DK)	70, 71, 74
Novozymes A/S (DK)	72
Nucleus Capital AG (DE)	64
Oncopeptides AB (SE)	28
Otsuka (JP)	6
Paleo BV (BE)	60
Patient Square Capital (USA)	74
Pfizer (USA)	13, 28, 77
Pheida AG (CH)	62
PhoreMost Ltd. (GB)	73
Pili (FR)	66
PlasmidFactory GmbH & Co. KG (DE)	81
Premier Research (USA)	15
Processium (FR)	67
Regeneron Pharmaceuticals Inc. (USA)	28
ReiThera Srl (IT)	76
Resolve Biosciences (DE)	74
Revier Therapeutics (DE)	74
Rewind Therapeutics (B)	46
REWOW (IT)	65
Ribbon Biolabs (AT)	85
Roche AG (CH)	6, 74, 75
Roquette Group (FR)	68
Sanifit Therapeutics (ES)	76
sctbio (CZ)	39
Seagen (USA)	13
Shimadzu Europa GmbH (DE)	CP2
Sibylla Biotech (IT)	76
Sierra Oncology (USA)	14
Sino Biological Europe GmbH (DE)	9, 88
Sobi AB (SE)	77
Sofinnova (FR)	68
Solar Foods (FI)	64, 71
Stalicia SA (CH)	73
Standing Ovation (F)	26, 27, 60
Strategic Consulting	44
Swiss Biotech Association, SBD (CH)	52, 53, 84
Telix Pharmaceuticals Ltd. (AUS)	29
Toulouse White Biotech, Æi TWB (FR)	65, 66
Trillium Therapeutics (USA)	14
Truffle Capital (FR)	68
Turning Point Therapeutics (USA)	14
Ucaneo Biotech GmbH (DE)	60
Univercells SA (BE)	73
Valneva SE (FR/AT)	46, 75
Ventus Therapeutics (USA)	70
VERISTAT International Ltd (UK)	41, 44
Vertex Pharmaceuticals Inc. (USA)	18
ViaCyte (USA)	18
Vienna Textile Lab (AT)	75
Vivescia (FR)	68
Volkswagen AG (DE)	64
Zymvol (ES)	68

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