

Dear friends and collaborators,

This special edition of our newsletter will summarise recent events and achievements involving KREATiS over the last year. The year 2020, despite the unfortunate turn of events experienced across the world, has clearly not diminished the desire of companies, regulators and academics alike to advance our understanding of intrinsic properties of the molecules we produce and use on a daily basis. Quite the opposite, it has perhaps highlighted the fragility of our globe and pushed us to take more care in the way we assess cost and benefits to human health and environment.

In brief, the last 12 months have been remarkable for KREATiS. During this time (and most recently) we have become a truly independent, privately owned, R&D organisation, perhaps the only one of its kind on the planet; we have received OECD recognition of the MechoA profiler which is currently being included in the OECD Toolbox; we have recruited a 3D modeller and invested in super-computer hardware to boost our digital revolution technology; we have worked on a battery of tests to provide strong evidence of the potential for endocrine disruption (or indeed, the lack of it!) in a diverse range of organic molecules; and won an exciting challenge open to start-ups across the globe.

Last year we rolled-out and have tirelessly continued to work on our new desktop version of iSafeRat[®], which has now become the mainstay of our High Accuracy QSAR modelling suite; and still on the desktop version, we have just released the biggest update ever on the iSafeRat[®] software. For the rapidly increasing number of you who have become iSafeRat[®] Desktop users, you will have automatically received the new downloadable version 2.0.10. Finally, we have continued to collaborate in research projects and diverse publications in both environment and human health.

KREATiS GOES INDEPENDENT

L'Isle d'Abeau (38), France:

On 7 August, 2020, KREATiS SAS, a subsidiary of the CEHTRA group, underwent a management buyout. The spin-off by CEHTRA represents a strategic decision to:

- Empower KREATiS with total autonomy, including expanding its partnerships and accessing new sources of funding for its ambitious research program.
- Leverage CEHTRA's consultancy expertise on behalf of its clients and continue to deliver industry leading solutions.

Xavier Dennery, President of CEHTRA said: "CEHTRA is proud of the progress made by its subsidiary KREATiS, which has now become a major player, and to which CEHTRA wishes all possible success. We are confident in the talent of the KREATiS team to enable it to carry out its many ambitious projects."

Paul Thomas, president and founder of KREATiS who, returning to his passion for the science of *in silico* modelling in the service of human health and the environment, highlighted "the great adventure shared with CEHTRA for 12 years, which now continues in different directions. We are looking forward to putting all our energy into new and exciting projects in the area of alternative testing methods."



NEW RECRUIT



Meet **Zlatomir TODOROV** our new PhD recruit! (Click [here](#) for a short CV).

Zlatomir finished his PhD in structural biology and nanobiology using molecular modelling in the middle of last year. Since then he has been working tirelessly for KREATiS on an EATS receptor database as part of our drive to create a battery of tests capable of discerning if substances have or do not have endocrine disrupting potential. This complements the work outlined in the **Endocrine Disruption** section below....

KREATiS "MechoA" PROFILER ACCEPTED BY OECD

The KREATiS MechoA profiler has been accepted for inclusion in the OECD toolbox. The Mechanisms of Action (or MechoA) profiler, is a decision tree based structural alert scheme that we have automated and made available as freeware on several platforms (currently you can find it on One Angstrom's SAMSON platform (www.samson-connect.net) and on the iSafeRat® Online website) and it is shortly to be released as a downloadable module on the latest version of OECD Toolbox where it is currently in beta testing.

We hope it will be ready for download before the end of this year.



LOGO REVAMP



It's not every day you buy a company so we decided that it was the moment to take a fresh look at our logo making it closer to the new image of the company, that is to say, sleeker, more efficient, modern and technologically dynamic than ever before.

We decided to maintain the graphical axes of the stem of the K and the grey underscore while refining the arrow to enhance the strong data driven core values of the company. We added an artistic flourish to the S at the other extreme of the logo which relates to our desire to apply innovative, out-of-the-box thinking to our solutions. We'd love to get your feedback on our new version.

By the way, we decided to keep our current slogan "Replacing Experimentation"... With the emphasis really being on vertebrate animals, of course.

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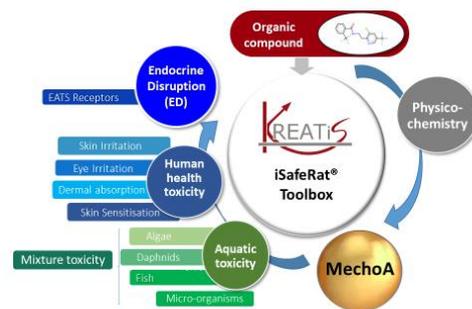
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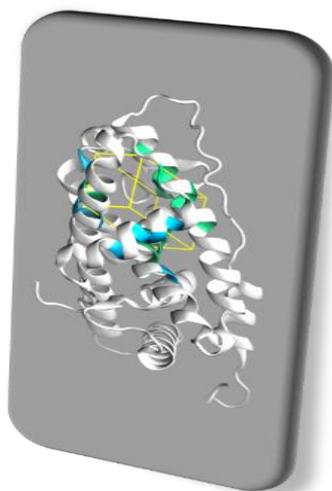
iSafeRat® UPDATE

Announcing the biggest update of the iSafeRat® algorithms ever released with a combined total of 2 years of work effort. We have now moved to iSafeRat® Desktop version 2.0.10 where we have:

- 1) The latest version of the SMILES structure scheme and provide 2D structure in real time;
- 2) Included over 40 new structural groups, notably high accuracy algorithms for log Kow, solubility and vapour pressure for multiple new substituents with a special emphasis on oxygen and nitrogen based compounds;
- 3) Continued work on our MechoA sub-class QSARs for acute and chronic toxicity to fish, daphnids and algae. Much of this work focussed on creating High Accuracy QSARs (HA-QSARs) especially for reactive substances.



ENDOCRINE DISRUPTORS: A DIGITAL DISRUPTION CHALLENGE



How do we tackle the challenges proposed by the European Parliament in their resolution adopted in 2019 calling on the Commission to **“swiftly take all necessary action to ensure human health and the environment are protected”** from EDCs? There are over 100 000 chemicals commercially sold and the vast majority have no useful data for EDC detection at all. But at the same time it is likely that many chemicals have no potential for endocrine disruption at all. How do we separate the wheat from the chaff?

KREATiS proposes a strategy that should help speed up the decision on prioritisation: A test battery integrating different in silico approaches (notably in-house (Q)SARs with 2D, and 3D “docking” models molecular modelling as used in drug design and third party tools) together these can predict the potential for molecules to form molecular complexes with receptors leading to **agonistic** or **antagonistic activity** or indeed, the **lack of potential to cause an effect**. This approach can help prioritise or deprioritise organic chemicals for further research.

The first 2 parts of the battery are already in service with satisfied customers submitting our reports to the authorities. In a few months we will be able to provide a 1st stage molecular docking service as part of our 3D modelling pipeline.

AND FINALLY: KREATiS WINS BAYER CROP SCIENCE HELLO TOMORROW CHALLENGE

Bayer Crop Science’s ambitious Open Innovation Programme to actively shape the future of agriculture recently led to an international startup call powered by Hello Tomorrow focussing on disruptive technologies and collaborations to help farmers, consumers and the planet! 124 start-ups from around the globe proposing solutions in digital phenotyping and in silico toxicology submitted applications and KREATiS was selected as one of the 6 finalists to present our offer on the 22nd October. After a nail-biting afternoon KREATiS was selected by Bayer as the challenge winner with Agrosage voted by the audience as runner up. KREATiS is looking forward to the next steps of a collaborative project with Bayer Crop Science aiming at a new level of High Accuracy QSARs in the challenging applicability domains of plant Protection Products.

We hope you have enjoyed this newsletter. We’ll be back in the New Year with more info on our activities. In the meantime, we would be delighted to receive your feedback. All the best from Paul and the KREATiS team