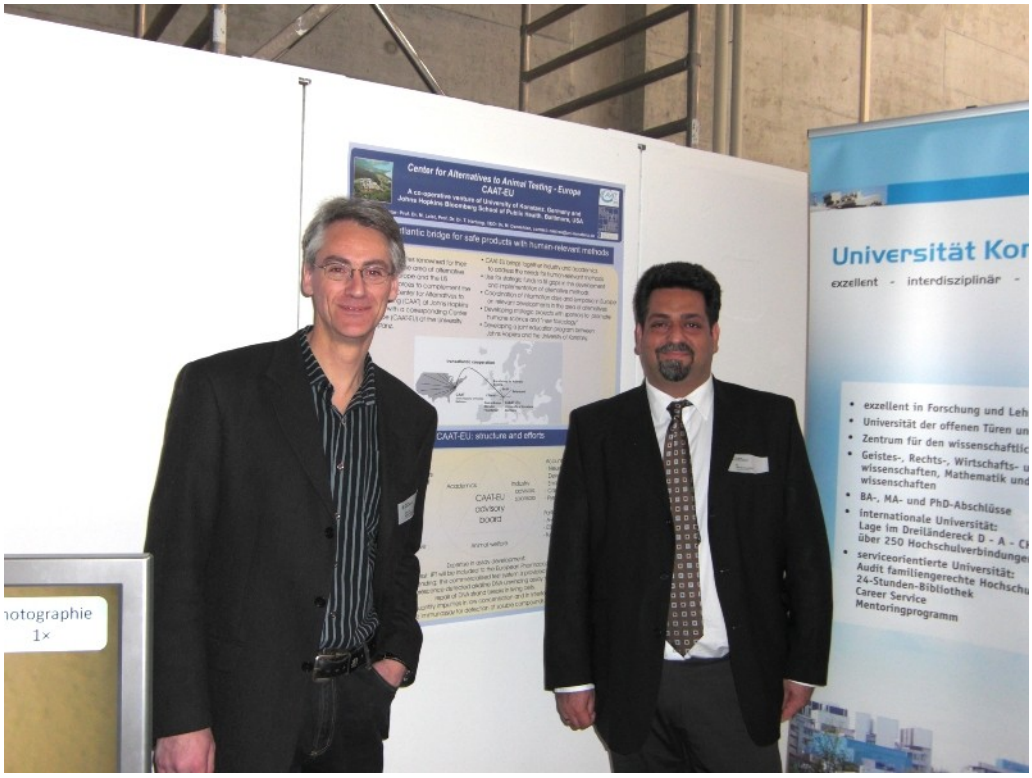
Healthcare industry BW

A long path from development to worldwide acceptance

In cooperation with the Johns Hopkins Bloomberg School of Public Health Baltimore, the University of Constance has established the Centre for Alternatives to Animal Testing – Europe (CAAT-EU) in Constance. The goal of the transatlantic cooperation is to establish new and innovative methods to replace the use of laboratory animals in studies, to combine the skills of the partners to provide a better, safer and more human future for humans and animals, and to become a communication platform for the global agreement on the harmonisation of safety tests. BIOPRO spoke with the head of the new competence centre and holder of the Doerenkamp-Zbinden Chair for In-Vitro Toxicology and Biomedicine, Prof. Marcel Leist (ML), and the managing director of CAAT-EU and biologist, Dr. Mardas Daneshian (DA) about the background and the vision of a worldwide standard for safety tests that looks to be within reach.



Prof. Marcel Leist, head of CAAT-EU and Dr. Mardas Daneshian, managing director of the new competence Centre for Alternatives to Animal Testing.
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Dr. Daneshian, for what reasons was the CAAT-EU established at the University of Constance rather than at any other university?

DA: Being one of the nine German Excellence Universities, the University of Constance can look back on a long tradition of in-vitro pharmacology and in-vitro toxicology. In addition, the University of Constance is the first university in Europe that has a chair of in-vitro toxicology and biomedicine. This biomedical focus, which is unique in Germany, and the 20-year tradition in the research and development of alternative test methods make the University of Constance the ideal location for the CAAT-EU.

Were new rooms and personnel required in order to establish the new centre?

DA: CAAT-EU is a think-tank and platform for communication between industry, science, animal protection organisations and governments. The centre is financed with funds from industry and the Doerenkamp-Zbinden foundation. The centre did not require any new rooms to be set aside for its establishment, as it is coordinated and run from the rooms of the CAAT-EU's directors, Prof. Marcel Leist and Prof. Thomas Hartung.

CAAT-EU is modelled after the Bloomberg School's Center for Alternatives to Animal Testing (CAAT). What does this mean?

DA: The Bloomberg School's Center for Alternatives to Animal Testing (CAAT) is based on a unique and successful organisational model, which has been reproduced at the CAAT-EU. It brings together experts from science, industry, government and more than 30 animal protection organisations (including the umbrella group, EuroGroup for Animals), thus enabling the direct flow of information. The strengths of the concept are that methodological weaknesses can be discussed and identified by the scientists, governments are involved in the processes being discussed as well as in the problems faced by industry and science, animal protection organisations talk with industry and also participate in the effort by industrial concerns to develop alternative methods to animal research.

Is the development of new methods to replace animal testing done jointly with the Johns Hopkins University?

DA: The two centres will work closely together in terms of science and the distribution of tasks. One of the advantages of this transatlantic cooperation is the excellence of the scientific expertise, because the cooperation and exchange of experience between experts from the USA and Europe will lead to synergies. In addition, innovative and conceptual achievements from the USA and Europe will be discussed and disseminated in the form of conferences and workshops on both sides of the Atlantic.

To what extent does the team of CAAT-EU have an interdisciplinary character?

DA: CAAT-EU works across almost all disciplines and is a European-wide organisation that deals with a broad range of different disciplines, including toxicology, vaccine development, the testing of seafood and fish, the quality testing of medicinal products and pharmacological efficacy tests. Besides the group of researchers led by Prof. Marcel Leist and Prof. Alexander Bürkle (head of the Department of Molecular Toxicology), the founding members of CAAT-EU also include Daniel Dietrich (human and environmental toxicology) and Prof. Hartung, honorary professor of pharmacology and toxicology. The core competences are complemented by an advisory board consisting of a broad range of different experts.

In addition to Prof. Marcel Leist, the CAAT-EU will also be directed by Prof. Thomas Hartung, honorary professor at the University of Constance.

The goal of CAAT-EU and CAAT is to develop a worldwide standard for the testing of chemicals: what form does the standard take and what are the major requirements?

DA: The two centres support the development of worldwide standardised alternative methods for the testing of chemical substances. Since the effectiveness of toxic substances is defined by the structural and functional changes in biological systems, the research and catalogisation of systems biology, genomic and metabolomic parameters that reveal such changes are self-evident. The vision of a worldwide standard for safety tests, which appears to be close to becoming reality, is characterised by the application of in-vitro high-throughput methods that are close to humans, i.e. actually work with human cells, cell cultures and organs, and focus on specific parameters that, according to our present state of knowledge, provide information about the toxicity of substances using in-vitro tests.

Prof. Leist, why does it take such a long time for alternative methods to be approved around the world, for example the alternative to pyrogen testing?

ML: These types of tests are used to identify undesired effects of chemicals, pharmaceuticals and cosmetics. Since these tests are carried out to test the safety of drugs, for consumer protection as well, the methods used to assess the toxicity of substances must be absolutely reliable. Therefore, new methods undergo thorough validation prior to granting approval. They are also tested in round robin tests in several independent laboratories in terms of feasibility and reproducibility. The methods can be optimised and tested again. And this must be done not only on the European-wide level, but also worldwide, and it must be included in the OECD guidelines and other directives. Nationally restricted approvals of alternative methods make no sense and would not lead to the phasing out of animal experiments. This is because companies that are supplying the world market would nevertheless be obliged to carry out animal experiments to seek approval in other countries.

Are there any promising methods that you believe meet future requirements and on which you would like to focus?

ML: CAAT and CAAT-EU support all promising developments, not only in the area of toxicology, but also in other areas of biological and biomedical research. Efforts to place the foundations of toxicology on a new basis are of particular interest. This implies not only the replacement of individual animal experiments, but also the establishment of approaches to safety testing on the basis of mechanistic experiments involving cells and primitive organisms. The development of in silico methods goes hand in hand with these developments, in order to determine the priorities for tests, if, for example, not enough test capacity is available, and also with regard to chemical testing according to REACH.

Do you work intensively with industry?

ML: Yes, we work very closely with industry. It is worth noting that the centres are financed by industrial partners and private institutions (e.g., Doerenkamp-Zbinden foundation) that act as sponsors and fund givers. Industry is an important developer as well as user of alternative methods. In addition, the companies have valuable experience in the advantages and disadvantages of animal experiments. Moreover, the experience of industry in terms of regulatory requirements is immensely important for developing new and acceptable alternative methods. CAAT-EU acts as a hub and discussion platform for the partners to exchange information, identify methodological gaps and work out solutions.

Prof. Leist, one of your projects deals with the development of a cell culture model for tests in which cell lines are brought into contact with substances. How do you investigate the influence of chemical substances, for example, on early embryonic development?

ML: We are working with embryonic stem cells of humans and mice. Depending on the protocol used, these cells can differentiate into all known cell types. We are particularly interested in neuronal development. By reconstructing this process in the test tube, just like the development of an embryo, we can specifically investigate the stages and steps that are negatively influenced by chemicals.

What were your recent findings?

ML: We know that chemicals such as mercury have a negative effect on the development of the nervous system in extremely low concentrations. Such concentrations are not detected by other toxicity tests since the substance does not have a damaging effect on the cells. This is alarming since the developmental disorders of the nervous system are not specifically investigated within the framework of normal safety evaluations.

In which fields will laboratory animals continue to be used in the future?

ML: I think laboratory animals will be used in research on animal physiology, in many fields of basic biological and pharmacological research, especially brain function. Here the key is to apply the 3R principle (reduce, replace, refine), according to which tests that still require the use of laboratory animals seek to reduce the animals' pain and suffering as much as possible by using non-invasive methods. Such methods include imaging methods used in medical applications, for example ultrasound and computed tomographies.

Further information:

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