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Aristides M Tsatsakis, Toxicol Open Access 2017, 3:1 (Suppl)
http://dx.doi.org/10.4172/2476-2067.C1.001

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Current status and challenges for toxicology and risk analysis in 21st Century: Integrating epidemiology experimental and computational data in real life exposures

Linking xenobiotic chemical exposure to health effects and diseases has been the subject of many experimental and epidemiological studies, though this issue remains a matter of permanent discussion and controversy. This issue is complicated by the multiple mechanisms of xenobiotic toxicity often involved, the uncertainties related to long term and low dose xenobiotic exposure, and the reliable identification of exposed and control groups. Exposure scenarios simulating real life is a complex issue as effects from multiply chemicals must be considered as a web of interactions that produce variety of mechanisms of effects and subsequently of health outcomes. In this respect linear –monomodal but also nonlinear effects can be seen in the range of low and/or high concentrations of exposures. Evaluating exposure effects is considered a multifactorial task that needs an integrated and systematic approach not only for long term actions but often for acute or sub chronic actions. Since such evaluations are highly work load and time consuming a sophisticated approach to identify the dominant actions and effects are in need. Real life is a variability and diversity of exposures the overall effect of which are pending on the certain case. Chemicals in general have a major impact on human and ecosystem health and highlighting the increasing need for effective and integrated means of risk assessment and exposure evaluation in human populations and biological ecosystems is crucial. This is not a trivial task and requires not only biomonitoring and exposure assessment but also combination of risk assessment with regulatory measures and actions. Harmonization in study methodologies by implementing OECD's adverse outcome pathway (AOP) approach and systematic dealing with confounders is required for a better characterization of exposure and understanding of the effects. Thus, the complex issue of links between chemical exposures and health problems and diseases is associated with multiple factors that are due to the expanding numbers of the chemical categories being present simultaneously or sequentially, the variety of mechanisms, mode of actions, adverse outcome pathways and effects involved but also on a large number of con-founders and also not less important to be encountered susceptibility due to genetics and epigenetics. Several epidemiological studies but also *in vivo* and *in vitro* experimental works showed that big majority of man produced consumer products even for dietary or life style purposes were found to act as endocrine disruptors, neuro developmental toxicants, immune toxicants and carcinogens in animals and humans. The general population experiences uncontrolled multi-chemicals exposure from many different sources at doses around or well below regulatory limits. Therefore, traditional chronic toxicity evaluations for a single chemical could possibly miss to identify adequately all the risks. For this an experimental methodology that has the ambition to provide at one strike multi-answers to multi-questions is hereby proposed: a long-term toxicity study of non-commercial chemical mixtures, consisting of common everyday life chemicals (pesticides, food additives, life-style products components) at low and realistic dose levels around the regulatory limits and with the simultaneous investigation of several key endpoints, like genotoxicity, endocrine disruption, target organ toxicity including the heart and systemic mechanistic pathways, like oxidative stress. In real life, the consumer is exposed to complex mixtures of chemicals via food and water consumption and via commercial products. Risk assessments, in general, however, focus on individual compounds. Therefore, the current regulatory approach does not assess overall risk in a highly relevant manner. This study will evaluate the cumulative toxicity of mixtures of different classes of pesticides alone and mixtures of different classes of pesticides together

with food additives and common consumer product chemicals in more realistic doses after long term exposure. If the hypothesis of an increased risk or even a new hazard not currently identified from cumulative exposure to multiple chemicals were shown to be true, this will provide further information to public authorities and research communities supporting the effort to replace today's single-compound risk assessment with a more robust cumulative risk assessment paradigm. Taking into consideration most recent aspects for risk assessment of individuals, where exposure assessment is personalized, we can realize the grounds and causation of the incomprehensible and hazy picture we face in our toxicology evaluations and the timely disagreement in facts among governmental and other international and authorial regulatory organizations throughout the world. It is a fact that as we expand the sphere of our knowledge in general we simultaneously expand the borders of our knowledge with ignorance. Being highly respectable to Socrates I suggest that the above sentence takes a step forward and clarifies for the public the deep meaning of the Socrates statement "I know nothing except the fact of my ignorance".

Biography

Professor Aristidis Michael Tsatsakis is the Director of the Department of Toxicology and Forensic Sciences of the Medical School at the University of Crete and the University Hospital of Heraklion. He is teaching the toxicology course for medical students for 30 years and specialization toxicology topics for postgraduate programs in few universities and supervised numerous PhDs. He received his PhD in Chemistry from Mendeleev University in Moscow 1986 and defended the title of Doctor of Science in Biology in University of Friendship of Nations in Moscow 2004. Prof Tsatsakis has written over 360 peer reviewed publications in prestigious journals, is holder of several patents and has given numerous lecturers as keynote and plenary speaker in international congresses. He has coordinated as PI over 40 scientific research and technology national, EU and international projects and established worldwide collaborations.

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