OECD-based hazard characterization of 2D materials at the skin level

Marco Pelin[1]
Michela Carlin[1], Silvio Sosa[1], Aurelia Tubaro[1], Maurizio Prato[2]
[1] *Department of Life Sciences, University of Trieste; Trieste, Italy*
[2] *Department of Chemical and Pharmaceutical Sciences, University of Trieste; Trieste, Italy*
mpelin@units.it

Abstract

Safety issues of 2D materials (2DM) for human health are mainly associated with an occupational exposure during their manufacturing as well as with consumer exposure in case of 2DM-based commercialized technologies. In this context, cutaneous contact is certainly one of the most important exposure routes. Beyond graphene-related materials (GRMs), several other 2D materials are currently exploited in this sector, such as transition metal dichalcogenides (TMDCs, such as MoS_2 and WS_2), hexagonal boron nitride (hBN), MXenes and black phosphorus.
This study took GRMs as reference 2DM to set up a case study to investigate the hazard posed by these materials at the cutaneous level focusing on the three main adverse outcomes: skin irritation, corrosion and sensitization. Their assessment was made through the application of specific test guidelines (TG) given by the Organization for Economic Co-operation and Development (OECD) to obtain robust and reliable toxicological data. In particular, skin irritation and corrosion were assessed following the OECD TG 439 and 431, respectively, using the SkinEthic™ Reconstructed human Epidermis (RhE) model, a fully differentiated 3D epidermal tissue constituted of normal human keratinocytes grown at the air–liquid interface. Skin sensitization was firstly assessed through the application of three *in chemico/in vitro* OECD TGs able to predict the first three key phases of skin sensitization Adverse Outcome Pathway (AOP), namely peptide reactivity (OECD TG 442C), keratinocytes activation (OECD TG 442D) and dendritic cells activation (OECD TG 442E). Subsequently, skin sensitization was evaluated also through an *in vivo* approach in mice, following the OECD TG 442B, able to predict the last skin sensitization AOP phase, namely lymphocytes activation.
All these guidelines, originally validated for chemicals, were assessed for their suitability to study also GRMs and, once applied, demonstrated that these materials appear to be non-irritant, non-corrosive and non-sensitizing at the skin level. Altogether, these results significantly contributed to shed light on safety issues associated with GRMs at the cutaneous level, finding a special importance for all those GRM-based technological applications implying a direct skin contact.