From scientific knowledge to regulatory application: the nanomaterial intestinal fate case study

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ABSTRACT

Nanomaterials (NMs) safety assessment is currently performed under the legal framework for chemical substances (e.g. REACH regulation, 1907/2006/EC). According to the revised REACH Annexes, specific requirements for testing NMs are still missing for some endpoints so the setup of international harmonized tools, as OECD Testing guidelines (TGs) and/or Guidance Documents (GDs), are strongly recommended. Several authorities, as EFSA and ISO, highlighted the relevance of NMs behaviour in the gastrointestinal tract (GIT) for the hazard assessment of ingested NMs. In this context, Italy leads an OECD proposal aimed to develop a new GD establishing conceptual framework and procedures for determining NMs fate in a simulated in vitro intestinal environment. The document considers the first steps of digestive process sequentially combining two in vitro approaches: 1) NMs fate in gastro-intestinal fluids along the different GIT compartments (mouth, stomach and intestine), and 2) NMs internalization and translocation through the intestinal barrier of the digested NMs. In step 1 the applicability to NMs of models for simulated digestion is taken into account, while an advanced intestinal in vitro barrier model is utilized in step 2 to investigate the interaction of digested NMs with the barrier. Final objective of the GD is to define the most reliable and robust tiered in vitro protocol, in line with the 3R principle, for studying NMs fate after oral exposure. In particular, a pilot study to standardize and optimize a tri-culture model of intestinal barrier is running at ISS. It is obtained co-culturing Caco-2 cells with other relevant intestinal cells as muco-secretory cells (HT29-MTX) and lymphoblastoid cells (Raji B). Even though this model is frequently used in evaluation of chemicals and NMs absorption, it shows quite variability which invalidate its wider application for regulatory purposes. Hence, the need to better establish experimental conditions and parameters.

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