One substance – Multiple assessments

Titanium Dioxide considered from a food and pharma perspective

On April 5th the section Pharmaceutical Toxicology and the section Risk Assessment organized a symposium entitled: “One substance – Multiple assessments” “Titanium dioxide considered from a food and pharma perspective”. The symposium was organized in a hybrid form. Around 30 participants attended the symposium on location at Leiden University. Whereas 55 participants attended online.

After a warm welcome of the chair for the day Susan Dekkers, the first speaker Joop de Knegt (RIVM) provided an introduction to the subject of the symposium.

Joop elaborated on the one substance one assessment (1S1A) approach by the European Commission. The approach aims at making the decision-making process more transparent, assessing chemicals in groups and coordinating safety assessments. There are initiatives to develop coordination mechanisms (cooperation between the European Commission, EU Agencies and EU member states is needed), CLP and REACH revision, horizontal legislative reallocation of the technical and scientific work, and developmental of tools and platforms. All initiatives around safety assessment of chemicals will be planned and includes all relevant regulatory frameworks through the public activity coordination tool (PACT). Furthermore, with use of an open data platform on chemicals, a single access point for the data and information on chemicals will be created, using IUCLID and providing guidance of better use of academic data in regulatory assessment (uniform format is needed).

The second presentation was provided by Jacqueline Castenmiller from the Office for Risk Assessment & Research of the Netherlands Food and Consumer Product Safety Authority. Before Jacqueline went into detail about titanium dioxide she provided some legal context regarding food (safety). In general food has to be safe (based on Regulation (EC) No 178/2002). The responsibility lies with the food business operators. Food additives can only be added to food when these are listed on appendix I and II of Regulation (EC) No 1333/2008. After this Jacqueline guided us through the reviews made by several agencies (NVWA-BuRO, ANSES, EFSA) and developments regarding titanium dioxide (E 171) which eventually led to the ban of E171 from food in 2022 based on the overall conclusion by EFSA that no threshold for TiO_2 could be established. At the start there were a lot of research questions that needed to be answered, but after the evaluation of EFSA of 2021, there are still many uncertainties with regard to the data used for the assessment, as e.g. the particle size and/or state of agglomeration, limited toxicokinetic data, toxicity at steady state.

The 3rd presentation was a co presentation by Ira Koval and Kim Nooteboom who are, respectively, preclinical scientific assessor and quality assessor at the Medicines Evaluation Board (MEB) in The Netherlands. It was made clear that contrary to food additives, a risk assessment of Titanium dioxide as excipient in medicines needs to take into account also the benefit(s) of its use, which will lead to a different risk assessment. Ira briefly touched on the guidelines that regulate potentially genotoxic and carcinogenic compounds as well as genotoxic impurities in medicines. She also pointed out that the use of colorants (like Titanium dioxide) in the EU is legally dependent on its authorization in food additives and that this legal construction is the root cause for the difficult position that pharma is having now. A ban of Titanium dioxide as food additive would (in principle) lead to a ban from medicines as well. Kim made clear that Titanium dioxide is more than just a colorant as it has a number of characteristics that are necessary to safeguide the quality of medicines. She also pointed out what the impact on medicines would be when Titanium dioxide was to be banned.

The fourth presentation was given by Marcel Kooij, who is a pharmacist in Amsterdam. His presentation started with an explanation of the role of the pharmacist, with extra emphasis of the importance of trust by the patient in the pharmacist and in the medication. Two recent cases were mentioned where the quality of medication came under discussion: nitrosamine impurities in several medications (such as Valsartan, ranitidine, metformine); and para-chloraniline in paracetamol. The recall of products which contained nitrosamine caused a lot of questions from patients, especially due to a communication from the Health Inspectorate which caused some confusion. It was recognized that any communication about a severe (but small) risk should be improved as much as possible, with the aim to inform patients in the best way, but also to advice patients whether they should continue or stop their treatment with this

medication. The case with titanium dioxide is potentially also causing the same kind of confusion in the public, but a pro-active approach from the pharmacists could help to minimize the confusion and to keep the trust that the public has in medications.

All presentations are available on the NVT website.