Metabolomics as read-across tool: a case study with phenoxy herbicides

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Abstract

The purpose of this paper is to provide a case study of how new technologies, such as metabolomics, can be used to address chemical grouping and read across from a biological perspective. To demonstrate this, we selected MCPP as the target substance and as source substances MCPA and 2,4-DP.

The 28-day metabolome evaluation of the source substances indicate the liver and the kidney as the target organs. The metabolome evaluation of the target substance provides the same information. The overall comparison of the metabolome data indicate that 2,4-DP is the best source substance. Using the information of the 90-day study of this compound, it would have been predicted that MCPP would have shown decreased food consumption and body weight gain at 2,500 ppm. The target organs are the liver (weight increase and clinical-pathology changes), as well as the kidney (weight increase and clinical-pathology changes). A moderate reduction of red-blood cell parameters would also be expected at this dose level. The NOEL would have been expected to be below the value of 2,4-DP, i.e. < 500 ppm and more likely in the range of that of MCPA, i.e. at least 150 ppm.

From a qualitative point of view, these predictions are very similar to the results of the actual 90-day study in rats performed with the target substance (reduced food consumption and body weight gain, target organs: liver and kidney – weight increases with concomitant clinical-pathology changes, reduced red blood cells values). From a quantitative point of view the predicted NOAEL of 150 ppm is in the range of that of the actual study (NOEL 75 ppm, NOAEL below 500 ppm). Thus, the 90-day rat toxicity study of the target substance could have been waived and substituted by the 90-day results of 2,4-DP. The NOAEL would have been correctly assessed as < 500 ppm, and using MCPA's values as at least 150 ppm.