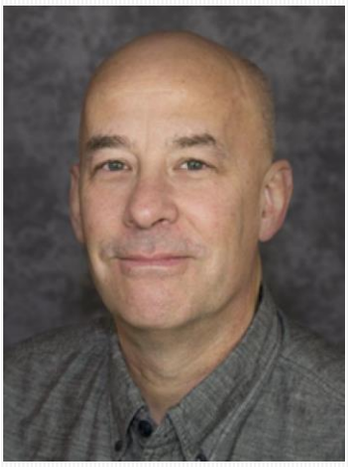
国立医薬品食品衛生研究所・特別講演会

日時

2024年12月3日（火）15:00 – 16:00



場所

国立医薬品食品衛生研究所2階【共用会議室】
神奈川県川崎市川崎区殿町3-25-26

講師

James Rathman, Ph.D. (Professor, Chemical and Biomolecular Engineering, Ohio State University, USA)

タイトル

A New Paradigm for Prediction Using an Ensemble Read-Across Approach

要旨

In silico **approaches such as quantitative structure-activity relationship (QSAR) models and rule-based systems are often useful in assessing chemical safety. However, these approaches are not well-suited to endpoints where specific chemical mechanisms or biological modes of action are complex. Examples include point-of-departure (POD) values such as benchmark dose (BMD) levels for carcinogenicity and no-observed-adverse-effect level (NOAEL) for systemic toxicity. We describe here an approach for estimating POD values using read-across from an ensemble of analogs, where the suitability of each analog is evaluated based on its similarity to the target molecule in multiple dimensions (structure, topological and physicochemical, ADME properties, biological assays) as well as the quality of study data available for the analog candidate. Decision theory methods are applied to report quantitative measures of read-across reliability for each estimation. Carefully curated BMD and NOAEL datasets have been assembled and designed to enable read-across scenarios ranging from generic (e.g., is this target likely to be carcinogenic?) to highly specific (e.g., estimate a NOAEL or BMD for the target with focus on liver or kidney effects). We also illustrate how this approach can be used to fill data gaps to predict assay results. This work illustrates how new paradigms for prediction and estimation can be applied in next generation risk assessment.**

お問い合わせ

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