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CropLife Europe Letter on BMD Platform

Dear Roncancio-Pena,

I am re-initiating contact with you regarding EFSA's Benchmark dose (BMD) tool, following the letter sent on 10 July 2023.

I thank you for acknowledging receipt of this previous letter, however, CropLife Europe's Statistics group experts have been exploring, testing and using the R4EU Bayesian BMD platform and the BMDABMDR R-package over the past year and one major challenge that they keep having is the absence of transparent and well-documented version control. Whilst it is appreciated that previous versions are now stored on GitHub with a note stating what has been updated, there is still no thorough documentation available regarding the changes and their impacts.

Crucially, in many cases, it is not clear whether an update is purely cosmetic or could have an impact on the BMD endpoints themselves. We have, for example, encountered notes such as "*implemented anydoseresponseQ without using 'brms' package"* and "*fix error in modelTest()*", which are not sufficiently informative. Similarly, in some instances, the BMD endpoints change after an update, but it is not clear why they have changed. Sometimes, it is also not clear whether the change is caused by updated methods, a bug being fixed or a new bug being introduced.

In line with analytical methods and analytical verification provided within the regulatory context, the mathematical and statistical models used also need a validated framework in place, which demonstrates accuracy, precision, reliability and repeatability. Together with transparency and traceability of what has been done, and why, these major aspects help to create robust and reliable statistical work for risk assessment and subsequent dossier submissions. A well-documented version control is an important step to accomplishing these aspects, and, therefore, vital to be included.

Furthermore, the absence of a proper version control is particularly problematic as it may lead to discrepancies between results when applicants submit BMD analysis conducted in one version, but authorities review results using a more recent version, due to the time gap between submission and authority review. Moreover, currently software versions change frequently, and changes are not always synchronised between R-package and online tool, thus leading to uncertainty about whether the results will still be accepted at time of submission.

Given this, it is important to clarify that dossiers should be reviewed using the same version as was available at the time of submission. Alternatively, applicants need to be given time to recalculate BMD endpoints and risk assessments if a new version leads to different BMD endpoints. To that end, it would be beneficial if online tool and R-package version updates are synchronized, and the version information is included and aligned in outputs. A timestamp may also be helpful when authorities later need to check which version was used.

CropLife Europe remains available if further information is needed and we hope that the above-mentioned issues are addressed.

Yours sincerely,

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Cc: Manuela Tiramani (EFSA)

This letter will be published on the CropLife Europe website and will be available at:
https://croplifeeurope.eu/resources-library/