Table S1. Risk of Bias Assessment. Reporting quality of all included *in vivo* studies.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author Year  Questions | Hou *et al*. 2021 [1] | Li *et al*. 2020[2] | Zheng *et al*. 2021[3] | Sun *et al*. 2021[4] | Chen *et al*. 2020[5] | Wang *et al*. 2021[6] | Capó *et al*. 2021[7] | Zhang *et al*. 2021[8] | Jin *et al*. 2021[9] | von Moos *et al*. 2012[10] | Zhao *et al*. 2021[11] | Xie *et al*. 2021[12] | Lu *et al*. 2021[13] |
| Was the test substance identified? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is the purity of the substance given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is information on the source/origin of the substance given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | X | √ | √ |
| Is all information on the nature and/or physic-chemical properties of the test item given, which you deem indispensable for judging the data (see explanation for examples)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is the species given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is the sex of the organism given? | √ | √ | √ | √ | X | √ | X | √ | √ | X | √ | X | √ |
| Is information given on the strain of test animals plus, if considered necessary to judge the study, other specifications (see explanation for examples)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is age or body weight of the test organisms at the start of the study given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | X | √ | √ | √ |
| For repeted dose toxicity studies only (give point for other study types): is information given on the housing or feeding conditions? | √ | √ | √ | √ | √ | √ | √ | √ | X | √ | √ | √ | √ |
| Is the administration route given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are doses administrated or concentrations in application media given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are frequency and duration of exposure as well as time-points of observations explained? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Were negative (where required) and positive controls (were required) including (give point also, when absent but not require, seeexplanations for study types and their respective requirements on controls)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is he number of animals (in case of experimmental human studies: number of test persons) per group given? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are sufficient details of the administration scheme given to judge the study (see explanation foe examples)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| For inhalation studies and repeated dose toxicity studies only (give point for other study types): were schieved concentrations analitically verified or was stability of the test substance otherwise ensure or made plausible? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are the study endpoint(s) and their method(s) of determination clearly described? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is the description of the study results for all endpoints investigated trasparent and complete? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are the statistic methods applied for data analysis given and applied in a trasparent manner (give also point, if not necessary/applicable, see explanations)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Is the study design chosen appropriate for obtainig the substance-specific data aimed at (see explanations for details)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| Are the quantitative study results reliable (see explanations for arguments)? | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| TOTAL | 21/21 | 21/21 | 21/21 | 21/21 | 20/21 | 21/21 | 20/21 | 21/21 | 20/21 | 19/21 | 20/21 | 20/21 | 21/21 |
| CATEGORY | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

√=yes; X=no

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