<u>APPENDIX 1:</u> Research Priorities - Design, conduct and reporting of clinical trials of cannabis, cannabinoids, and cannabis based medicines.

Future RCTs should strive to achieve pre-registration, obtain full ethical approval, adherence to trial protocols, target full and open reporting of data (not only mean change data), and allow access to individual patient data. Deviations from protocol and reasons for that deviation should be reported.

New RCTs attempting to demonstrate analgesic effectiveness in people with established pain must be of the highest standard, with adequate sample sizes, double-blinded to the possible extent, ideally multicenter, with and without adjunctive analgesic treatment, and conducted in people with moderate-severe pain from well-defined pain conditions. They would ideally involve patient partners in developing patient-centered and meaningful outcomes.

Multiple imputation methods should be compared and reported with a stated rationale for each.

Future trials should also include patients in low to middle income settings outside North America and Western Europe, and involve patient stakeholders.

Baseline patient-reported pain intensity \geq 40/100 VAS (or \geq 4/10 NRS), and careful baseline patient characterization (biopsychosocial and cognitive) are highly recommended.

Outcomes to include number of participants with 30% and 50% reduction in pain intensity (and ideally pain interference) with tolerable adverse events.

Full reporting of adverse events and withdrawals, with reason.

Full declaration of commercial and non-commercial interests held by the authors should be disclosed and declared. Any funding received directly for the study should be disclosed.