Executive Summary

Review of Results from

The Dosing Project™

Proof of Concept Phase

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Executive Summary

In the early 20th century, Cannabis entered a period of prohibition which suppressed clinical investigations on its safety and efficacy. At the turn of the 21st century, Cannabis use was again permitted and has spread throughout the globe. The Dosing Project™ is a crowd-sourced surveillance tool that takes advantage of a depth of historical use in order to understand Cannabis dosage, anticipated effects and adverse events. The Dosing Project™ surveys Cannabis users to inform on Cannabis dosage and adverse events with an intent to facilitate safety and optimal product development. Our surveillance approach captures real-world effects using a non-interventional, observational approach in a naturalistic setting. Commonly, Cannabis users describe two types of effects from different cultivars. The "Sativa" effect is energetic and is associated with an anxious experience. The "Indica" effect is sedative and is associated with a hypnotic experience. Since chemotypic categorizations may readily correlate with anticipated effects, defining a taxonomy that aligns with this popular perception is a major goal of the Dosing Project™.

Our initial investigations with the Dosing Project™ involved smoked or vaporized Cannabis flowers that were chemotypically distinct. The main Cannabis Phytocannabinoid classes (Type I, Type II, and Type III) provided a primary categorization of Cannabis flowers. Additionally, we approached the "Sativa" / "Indica" dichotomy through the application of community-derived aroma categorization ("Floral" and "Fuel", and included "Earth" for attenuated material). The Dosing Project™ specifically targeted two major indications, respondent-identified pain and disordered sleep.We collected self-reported height and weight to normalize the consensus cannabinoid content for each cultivar to the respondent's weight and determined a standard pharmacologic dose in milligrams per kilogram (mpk). Informed consent was obtained. The Therapeutic Response dependent variable was collected as a 4-level categorical response: "no improvement", "partial improvement", "almost complete improvement", and "complete improvement". Self-reported Adverse Events were collected as a closed set of entries eliciting a binary ("Yes" / "No") response.

Overall, the highly significant difference ($p<0.0008$) between the longer times of reporting for "Sleep" vs "Pain", supported the validity of the Dosing Project™ approach: since sleep-reporting should occur after sleeping. Difference in amount used for "Pain" vs "Sleep" was borderline significant ($p<0.0523$). Certain Adverse Event incidences differences signalled a potential utility of CBD. We have effectively established a valid dose-response relationship for inhaled Cannabis flowers through our statistical modelling. Additionally, the borderline significance of the interaction of CBD dose with aroma category suggests synergy or entourage effect underlies its mechanisms of action. For the "Earth" aroma category, we observed a highly significant logistic regression for facilitating a sleep response by THC dose; the median effective dose in the "Complete Response" cohort for THC mpk differed from that of the "Floral" aroma category. We observed significant CBD dose-responses for improving pain within certain of the aroma categories; which suggested that the overall dose-response relationship may be biphasic. We successfully used social media to drive recruiting into targeted responder cohorts and observed seasonal trends indicating the influence of harvest periods. Certain trends may reflect poor packaging and storage options available across the supply chain. Ongoing work at the CESC is aimed at identifying best practices that mitigate such product attenuation, and will be the subject of a forthcoming report.

In summary, we propose a pre-IND Phase I observational study for investigating Cannabis dose, effect and adverse events. The Dosing Project™ will incorporate marketed Cannabis products with batch associated laboratory data, expanded routes of administration, expanded Indications, expanded demographic queries (age, gender), and an emphasis on longitudinal analysis. Advanced product study includes subjective scale surveys and physiological biomarkers. The Dosing Project™ establishes Cannabis product certification for public safety and dose efficacy.