

# The Results of a Multi-Company Validation of the ActualHCA™ Home Cage Monitoring System for Rodent CNS Safety Pharmacology Studies

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**Introduction:** Traditional core battery CNS safety pharmacology assessment relies on the FOB/Irwin, a subjective behavioral screen including a panoply of rodent-specific parameters that are difficult to translate to human outcomes. Home cage monitoring systems objectively measure continuous rodent behavior, day and night, over multiple days. The welfare benefits of the approach, which allows group housing and non-invasive monitoring, are established. However, the value of these data in CNS safety assessment compared to those obtained from the FOB/Irwin remains largely untested.

The aim of this collaborative work was to assess the potential of rodent home cage monitoring, using a few key parameters (locomotor activity, rearing and body temperature), to better predict risk over traditional FOB/Irwin. Three compounds (GSK, JNJ and AZ), for which findings have previously been reported in FOB/Irwin and clinically (GSK and AZ), were tested using the home cage monitoring system and the data were analyzed.

**Methods:** For each test condition, six male Han Wistar rats (sourced from Charles River UK Limited, Margate) were implanted with temperature sensitive RFID transponders (BioMark USA) and housed 3 per cage. Cages were placed inside the home cage monitoring system and recorded for 10 days to provide an initial 4 days baseline measurement followed by the dose/treatment day and then followed by a further 5 days post-dose. In addition to the dosing procedure, a blood sample was taken within 24hrs. Both events are indicated on the plots. On post-dose day 3, the cages were changed.

For each animal, 3 days of pre-dose data are averaged to form a 24hr baseline profile. The continuous profiles (24hr or 5-day) show the behavioural profile recorded plotted alongside the baseline for reference. The bar graphs focus on specific time windows highlighted by a yellow overlay. The bars represent the difference between the observed measurements and the pre-dose baseline within the window of interest. Data were analysed using one way ANOVA, followed by Dunnett's test. Statistical significance was set at  $p < 0.05$ . All animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and local policies on the Care, Welfare and Treatment of Animals.

