Integrated *in vivo* Safety Pharmacology Study Developed for Investigating Effects of a Drug on the Central Nervous, Cardiovascular, and Respiratory Systems Simultaneously in Dogs, Monkeys, or Other Animals

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Current *in vivo* Safety Pharmacology Study

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<tr>
<td><strong>Irwin or FOB</strong></td>
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<td><strong>Telemetry</strong></td>
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<td><strong>WBP</strong></td>
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Central Nervous, Cardiovascular, and Respiratory Systems should be examined separately.
Disadvantages of Current *in vivo* Study

- Impossible to conduct WBP using large animal under ideal environmental conditions
- Make it difficult to predict clinical side effects on CNS, CV and RES
- Impossible to evaluate effects on CNS, CV and RES simultaneously
- Less efficient due to separate tests
- Unfavorable from animal protection stand point of view
Integration of *in vivo* Safety Pharmacology Study

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CNS, CV, and RES can be examined simultaneously!
Integration of *in vivo* Safety Pharmacology Study

- Preamplifiers
- ECG
- BP
- Air Filter
- Fan
- Telemetry Receiver
- Respiratory Air Flow
- Plethysmograph Computer
- Preamplifiers
- Computer
- DSTC, Drug Safety Testing Center
- Integration of *in vivo* Safety Pharmacology Study

**Diagram Description:**
- *ECG (Electrocardiogram)*: Signals related to the heart's electrical activity.
- *BP (Blood Pressure)*: Measuring the pressure of blood as it flows through blood vessels.
- *Air Flow*: Indicates the measurement of airflow.
- *Telemetry Receiver*: Receives signals from remote sources.
- *Plethysmograph Computer*: Used for measuring blood flow changes in a body part or region.
- *Preamplifiers*: Amplify weak signals before transmission.
- *Computer*: Processes and analyzes data from the various sensors.

**Context:**
- This diagram illustrates the integration of various components in a safety pharmacology study, emphasizing the measurement of physiological parameters in *in vivo* settings.
- *DSTC (Drug Safety Testing Center)*: A facility dedicated to evaluating the safety of new pharmaceuticals.

**Integration Details:**
- *Fan* and *Air Filter* are likely used for maintaining a controlled environment.
- *Telemetry Receiver* and other devices are connected to record and transmit physiological data.
External Appearance of Integrated \textit{in vivo} System
General Observation on the Central Nervous System

For an Animal Staying in the Cage

- Viability
- Posture
- Behavior
- Activity
- Central Excitation
- Convulsions

For an Animal removed to Outside of the Cage

- Muscle Tonus
- Righting Reflex
- Pupillary Reflex
- Palpebra Reflex
- Pinna Reflex
- Hearing Test
- Haptic Test
- Algetic Test
- Oculus
- Nose
- Mucosa
- Salivate
- Vomiting/Feces and Urine
Representative Data of Telemetry

Body Temperature

Activity

DSTC
Drug Safety Testing Center

Representative Data of Telemetry

Body Temperature

Activity

DSTC
Drug Safety Testing Center

(c) DSTC
Drug Safety Testing Center

(c) DSTC
Drug Safety Testing Center
Representative Data of Telemetry – Cont’d

Blood Pressure

Electrocardiogram

Intrapleural Pressure
Representative Data of WPB

Respiratory Air Flow

Penh, Room Temperature and Humidity

Tidal Volume

Drug Safety Testing Center
Summary

• WBP is available under less stressful environmental conditions
• Improve predictability of clinical side effects on CNS, CV and RES
• Simultaneous evaluation of effects on CNS, CV and RES become possible
• Facilitate evaluation and result in enhancement of efficiency of experiments
• Contribute to animal protection by reducing number of animals to be tested