The Impact of the Functional Observational Battery and Irwin Tests in CNS Safety Pharmacology: Results of an Industry Survey

Introduction

- The functional observational battery (FOB) and Irwin test battery (together called the ‘neurofunctional impactful’)
- These results will be further discussed in a Sponsored session on 3 November at the SPS Annual Congress.
- In this study, an international working group formulated and distributed a detailed survey to gather information on how the neurofunctional assessment is used within organisations, how the data is interpreted and opinions on the impact of individual measures.

Experimental Design in the Neurofunctional Assessment

H. Which sex of animal are commonly used in studies?
J. How many animals are used for each compound tested in the neurofunctional assessment?
K. Are observational or measured data subjected to statistical analysis?
L. In what percentage of studies is the neurofunctional assessment incorporated into a toxicology study?

Survey Respondent Demographics

- A. In which country do you work?
- B. What kind of organisation do you work for?
- C. What is the basis of the neurofunctional assessment used at your organisation?
- D. Is the neurofunctional assessment used as a standard tool to assess safety in small molecules, biotechnologies and cell-based therapies?
- E. Has a compound been stopped on the basis of the FOB/Irwin alone?
- F. Is the assessment performed (or repeated in the same species) to fulfill regulatory requirements?
- G. How often does the assessment contribute to a decision to stop a compound?
- H. In what percentage of studies is the neurofunctional assessment incorporated into a toxicology study?

Analysis and Ranking of Individual Measures in the Neurofunctional Battery

- A composite list of measures used in the neurofunctional assessment was created from published information.
- Respondents were asked to indicate how ‘impactful’ each measure is on decision making during drug development. Terms were defined as:
  - ‘impactful’: the impact of the measure(s) alone or in combination on decision making in drug development or candidate selection when using data from the neurofunctional assessment.
  - ‘effective’: a compound-related effect which is of note in the neurofunctional battery.
- The number of people responding to each category was then weighted:
  - Very impactful
  - Somewhat impactful
  - Not impactful
  - Not at all impactful

The Impact of the Neurofunctional Assessment on Decision-Making

M. Is the assessment performed (or repeated in the same species) to fulfill regulatory requirements?
N. Is non-GLP data presented to regulators?
O. How often does the assessment contribute to a decision to stop a compound?
P. In what percentage of studies is the neurofunctional assessment incorporated into a toxicology study?
Q. What percentage of assessments are predicted by a prior study?

Spare Animals in the Neurofunctional Assessment

- Do you order spare animals in case replacements are needed on the study?
- How often are spare animals used on a study?
- What is the fate of spare animals?
- In what percentage of studies is the result predicted by a prior study?
- In what percentage of studies is an effect seen in the FOB/Irwin?

Key Messages and Next Steps

- These results provide information on how the neurofunctional assessments are being used in drug discovery and early drug development, and present opinion from a cross-section of the industry on how impactful individual measures are on the decision making process.
- There is wide variability in the conduct of neurofunctional assessments across the industry and the impact of individual measures within these tests. It should be noted that, although defined in the survey, the term ‘impactful’ may have different interpretations.
- The neurofunctional assessment was designed to detect overt safety signs, but its efficacy at detecting less severe adverse or non-adverse effects has not been characterised.
- Some SPO opportunities have been highlighted through this data, including viable and large group sizes, the use of spare animals and repeating studies for regulatory submission.
- These results will be further discussed in a Sponsored session on 3 November at the SPS Annual Congress 2018.

References