

# Increasing signal detection in clinical trials: improving fidelity of instruments

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**Background:** Treatment effects in schizophrenia can be subtle. Even small imprecision in measurement can lead to false negative results. One strategy to improve measurement is to conduct consistency checks in the use of measures.

**Methods:** ISCTM (International Society for CNS Clinical Trials and Methodology) convened a working group of PANSS experts who assembled, over the last 2 years, consistency flags for the PANSS (Positive and Negative Syndrome Scale), 30 item scale, each item rated 1-Absent, 2-Minimal, 3-Mild, 4-Moderate, 5-Moderate-severe, 6-Severe and 7-Extreme.

Flags were rated by working group based on likelihood of being an error as “High”-Very probably (or definitely), “Medium”-probably and “Low”- possibly. Flags were applied to the NEWMEDS (121,635 assessments of 19,489 subjects and CATIE data 8,849 assessments of 1,450).

**Results:** Twenty-three flags were identified. Almost 40% of NEWMEDS and CATIE ratings had at least one flag raised, and approximately 10% had two flags raised.

**Conclusions:** Analyzing items within the PANSS, as well as comparing the PANSS items to ratings on other scales, can help to identify potentially incorrect ratings which may be remediated with rater training and could also be used to develop a metric for rater selection.

## Most common flags found in NEWMEDS and CATIE (>2%)

Most common flags	% NewMeds assessments/ % CATIE
Same response on 27, 28, 29 or all items from previous visit (High flag)	14%, 11%, 8%, 6% (not checked in CATIE)
N6 Lack of spontaneity 2 pts > than N3 Poor rapport (Low flag)	2% / 2%
If either Hostility or G14 Poor impulse control is at least 4 Moderate, then the others should not differ by more than 2 points (Medium flag)	5% / 4%
G4 tension should not be greater than anxiety (Medium flag)	17% / 14%
G6 Depression 5 Moderate-severe or greater, G7 motor retardation at least 3-Mild (Medium flag)	2% / 4%
P3 Hallucinatory behavior 5 Moderate-severe or greater, then G15 Preoccupation at least 5 Moderate-severe (Medium flag)	11% / 15%
P2 Conceptual disorganization 5 Moderate-severe or greater then N5 Difficulty abstract thinking at least 5 Moderate-Severe (Low flag)	5% / 4%

## Additional flags

High
Change from 1 to 7 or 7 to 1 on an item
P5 Grandiosity 5 Moderate-severe, 6 Severe or 7 Extreme must be 3 or greater on P1 Delusions
P6 Suspiciousness 6 Severe or 7 Extreme, must be 3 or greater on P1 Delusions
G1 Somatic concerns 6 Severe or 7 Extreme must be 3 or greater on P1 Delusions
G3 Guilt feelings 6 Severe or 7 Extreme must be 3 or greater on P1 Delusions
G9 Unusual thought 5 Moderate severe, 6 Severe or 7 Extreme must be 3 or greater on P1 Delusions
CDSS PANSS depression item discord <sup>1</sup>
Medium
CGI-S PANSS discord <sup>2</sup>
G7 motor retardation 6 Severe or greater; N6 lack of spontaneity must be 5 Moderate-severe or greater
N4 Passive Social withdrawal and G16 Active social withdrawal cannot both be 7 Extreme
G7 motor retardation of 5 Moderate-severe or higher and a score of 4 Moderate or higher on P4 Excitement
P5, P6, G1 and G3; no more than 1 can be 7 Extreme
Difference of more than 2 points between G8 Uncooperativeness and P7 Hostility
Low
Difference of more than 2 points between G8 Uncooperativeness and P7 Hostility
Hostility, Uncooperativeness and G14 Poor impulse control; if anyone is greater than 3 Mild then others should not differ by more than 2 points
P3 Hallucinatory behavior 5 Moderate-severe or greater then G15 Preoccupation at least 5 Moderate-severe

<sup>1</sup>Based on CDSS cutting points for clinical depression. PANSS depression item 1-Absent= CDSS 0 to 2, 2-Minimal=3, 3-Mild=4-5, 4-Moderate= 5-6, 5-Moderate Severe=7-9, 6-Severe=9 or greater. <sup>2</sup>Based on the literature the following PANSS ranges for CGI scores were derived CGI-S of 3 Mildly ill, PANSS range of 55 to 80; CGI-S of 4 Moderately ill PANSS in range of 71 to 92 and CGI-S of 5 Markedly ill with a PANSS in the 88 to 100 range.

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