Characteristics of Screens

An excellent introduction to the characteristics of screens in Redman's [10] interesting approach, which identifies four characteristics of an assay. Redman assumes that a compound is either active or inactive and that the proportion of activities in a compound can be estimated from past experience. After testing, a compound will be classified as positive or negative (i.e., possessing or lacking activity). It is then possible to design the assay so as to optimize the following characteristics:

1. Sensitivity: the ratio of true positives to total activities
2. Specificity: the ratio of true negatives to total inactives
3. Positive accuracy: the ratio of true to observed positives
4. Negative accuracy: the ratio of true to observed negatives
5. Capacity: the number of compounds that can be evaluated
6. Reproducibility: the probability that a screen will produce the same result at another time (and, perhaps, in some other lab)

An advantage of testing many compounds is that it gives the opportunity to average activity evidence over structural classes or to study quantitative structure–activity relationships (QSARs). Quantitative structure–activity relationships can be used to predict the activity of new compounds and thus reduce the chance of in vivo testing on negative compounds. The use of QSARs can increase the proportion of truly active compounds passing through the system.

To simplify this presentation, data sets drawn only from neuromuscular screening activity were used. However, the evaluation and approaches should be valid for all similar screening data sets, regardless of source. The methods are not sensitive to the biases introduced by the degree of interdependence found in many screening batteries that use multiple measures (such as the neurobehavioral screen).

1. Screens almost always focus on detecting a single end point of effect (such as mutagenicity, lethality, neurotoxicity, or development toxicity) and have a particular set of operating characteristics in common.
2. A large number of compounds are evaluated, so ease and speed of performance (which may also be considered efficiency) are very desirable characteristics.
3. The screen must be very sensitive in its detection of potential effective agents. An absolute minimum of active agents should escape detection; that is, there should be very few false negatives (in other words, the type II error rate or β level should be low). Stated yet another way, the signal gain should be way up.