

4. It is desirable that the number of false positives be small (i.e., there should be a low type I error rate of α level).
5. Items 2 to 4, which are all to some degree contradictory, require the involved researchers to agree on a set of compromises, starting with the acceptance of a relatively high α level (0.10 or more), that is, an increased noise level.
6. In an effort to better serve item 2, safety assessment screens are frequently performed in batteries so that multiple end points are measured in the same operation. Additionally, such measurements may be repeated over a period of time in each model as a means of supporting item 3.
7. This screen should use small amounts of compound to make item 1 possible and should allow evaluation of materials that have limited availability (such as novel compounds) early on in development.
8. Any screening system should be validate initially using a set of blind (positive and negative) controls. These blind controls should also be evaluated in the screening system on a regular basis to ensure continuing proper operation of the screen. As such, the analysis techniques used here can then be used to ensure the quality or modify the performance of a screening system.
9. The more that is known about the activity of interest, the more specific the form of screen that can be employed. As specificity increases, so should sensitivity.
10. Sample (group) sizes are generally small.
11. The data tend to be imprecisely gathered (often because researchers are unsure of what they are looking for) and therefore possess extreme within-group variability. Control and historical data are not used to adjust for variability or modify test performance.
12. Proper dose selection is essential for effective and efficient screen design and conduct. If insufficient data are available, a suitably broad range of doses must be evaluated (however, this technique is undesirable on multiple grounds, as has already been pointed out).

It should be kept in mind that there are a number of common mistakes (in both the design and conduct of studies and in how information from studies is used) that have led to unfortunate results, ranging from losses in time and money to the discarding of perfectly good potential drugs. Such outcomes are indeed the great disasters in drug discovery—especially since many of them are avoidable if attention is paid to a few basic principles.

It is quite possible to design a study for failure. Common shortfalls include:

1. Using the wrong animal model.
2. Using the wrong route or dosing regimen.