Compound Selection Guidelines

Structures are generally selected for screening based on their ability to add diversity to the NCI small molecule compound collection. The submission of novel heterocyclic ring systems is particularly encouraged. In addition, NCI60 encourages the submission of compounds with drug-like properties utilizing the concept of privileged scaffolds (1,2,3) or structures based on computer-aided design. The program is not intended to handle extensive supplier SAR studies that include large numbers of similar analogs. If analogs within a series are to be submitted, it is recommended that suppliers initially pre-select only the compounds within an analog series which will most efficiently provide the greatest information. This will ensure that the structures of most interest to the supplier are selected. If initial submissions show activity, they can provide a basis for the consideration of future analogs.

Highly flexible acyclic analogs with accompanying entropic liabilities are generally not accepted. Submission of structures containing problematic linkages or functional groups for successful drug development (e.g., nitro, nitroso, -N-N-, -N=N-, imine, semicarbazone, thioamides, thioureas) are discouraged. Analogs related to well-studied agents (e.g., brefeldins, anthracyclins, taxanes, camptothecins, combretastatin, aminoacridines, platinum-based agents) which have been the subject of thorough SAR investigations are also generally not selected without providing a rationale (or preferably data) for improved or novel biological or chemical properties which would support continuing development. As a service, the program also supports NCI60 cell screen characterization (e.g., tumor selectivity, COMPARE data) of important individual late pre-clinical or investigational clinical agents.

Pan-assay interference compounds (PAINS) with activity that does not generally depend on a specific, drug-like interaction between molecule and protein are also discouraged. A list of the most notorious PAINS include, but are not limited to, these chemotypes (Baell, J; 2014)

- Toxoflavins
- Iosthiazolones
- Curcumin analogs
- Hydroxyphenyl hydrazones
- Ene-rhodanines
- Phenol-sulfonamides
- Enones
- Quinones
- Catechols

The following classes of materials are generally not accepted:

- Radicals
- High MW pegylated or similarly derivatized agents
- Multiple pharmacophores linked by a tether(s)
- Physical mixtures of active components
- Reactive molecules, thermal or photo labile molecules (e.g., mustards, acyl halides, α-halo carbonyl compounds, reactive Michael acceptors)
- Nanoparticle formulations