

Application of 'Smart' High Throughput Technologies to Drug Substance and Drug Product Development.

Colin R. Gardner,
TransForm Pharmaceuticals Inc.,
610 Lincoln Street,
Waltham, Ma 03451.

The pharmaceutical industry has undergone very significant transitions in the last 25 years, starting with the application of the evolving biochemical understanding of the causes of disease, through the biotechnology revolution, the advent of high throughput assay methodology and chemical synthesis to the application of genomics to define potential targets for a drug discovery program. These developments have had a dramatic effect on the speed with which interesting, potent and selective compounds can be identified in large numbers. However, the very use of these technologies has resulted in compounds whose physical properties are very challenging and which pose significant difficulties for the development departments in the industry to convert them to “real drugs” which can be effectively absorbed to reach their intended target in the body. During this time period there has not been the same major change in the ability of the development groups to apply high throughput technologies to the drug development process. Consequently, these departments find themselves facing an avalanche of new chemical entities proposed as potential new drug candidates, but with properties that demand much greater and deeper evaluation, under the enhanced scrutiny of the regulatory agencies who demand that the materials used to determine the safety and efficacy of a drug product in clinical trials are directly correlated with those which the company ultimately takes to market.

TransForm Pharmaceuticals Inc was founded on the premise that the application of high throughput (HT) technologies could provide the development scientists with much enhanced capabilities that would permit them to make significant contributions across the drug discovery/development axis. By providing the ability to run parallel experiments on the order of thousands using sub-milligram amounts of material per experiment, applications were foreseen in:

- the identification of drug candidates with improved physical properties,
- the rapid discovery of physical forms of the active ingredient including salt forms, hydrates and solvates and polymorphic forms,
- the design of formulations with properties optimized for bioavailability and stability,
- the identification of methods to accomplish these goals,
- the provision of data to assist in scale-up of processes for drug substance and drug product to meet regulatory demands, and
- the ability to use informatics to mine the large amounts of data and develop correlations and knowledge which would permit smarter design of subsequent studies.

This presentation will show the reduction to practice of these concepts with a number of examples from across the drug discovery / development timeframe.