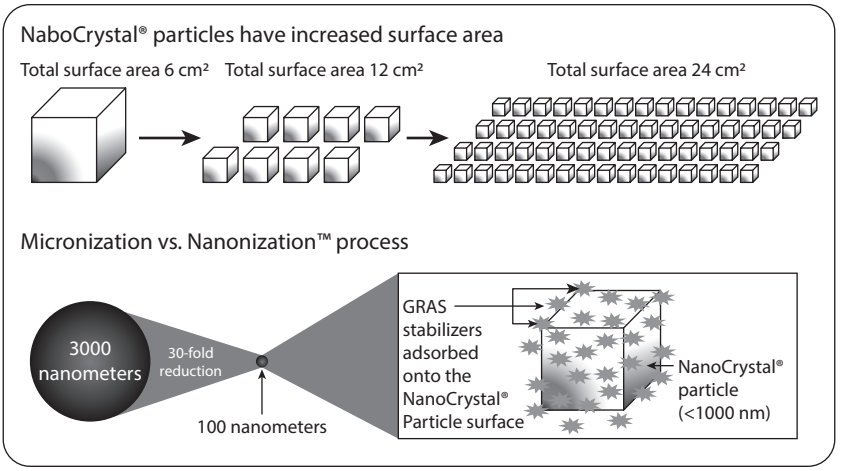

FIGURE 3.1 The NanoCrystal® technology. (Courtesy of Elan Corporation, Dublin 2, Ireland.)

Nanonization is a formulation technology that can be universally applied to all drugs—each drug can be transferred to drug nanocrystals. The main production technologies available to produce drug nanocrystals have their advantages and limitations. The reduction of solid particles to nanoparticles is achieved by high-pressure homogenization.

3.4.3 Salt Screening

Recent trends in combinatorial chemistry have resulted in the synthesis of large-MW lipophilic drugs. Converting the free acid/base form to a salt is an important option to explore when trying to improve solubility and oral bioavailability. Of the 21 new molecular entities approved by the FDA in 2003, 10 were salt forms. Selection of the right counterion with optimum physiochemical characteristics is crucial to drug development. Consideration of the new compound's physical–chemical properties, processability under various manufacturing conditions, and bioavailability must be made. A complete range of characterization tools for a complete salt screen would include the following:

- X-ray powder diffraction analysis (XRD)
- Thermal analysis (DSC, thermogravimetric analyzer [TGA], and thermomechanical analyzer [TMA])
- Microscopy (light and polarized)
- DVS—moisture absorption and desorption
- Density (intrinsic and bulk)
- NMR analysis
- Solubility analysis in various media
- Dissolution (including intrinsic dissolution testing)
- Particle size analysis (optical, laser light, and light obscuration)

Scheme 3.1 describes a salt-screening decision-making tree.