cloning made it possible for scientists to generate cell lines that overexpressed targeted biomolecules, essentially eliminating the supply limitations of the past. Recombinant proteins could be harvested from cellular factories, providing ample quantities of target proteins. Alternatively, custom cell lines could be designed to incorporate biomolecular targets to support cellular screening assays. At the same time, advances in the fields of computer science, robotics, and automation led to the development of robotic platforms capable of performing repetitive motion tasks previously handled by humans, increasing accuracy and efficiency of any number of tasks in multiple fields (Figure 2.17).

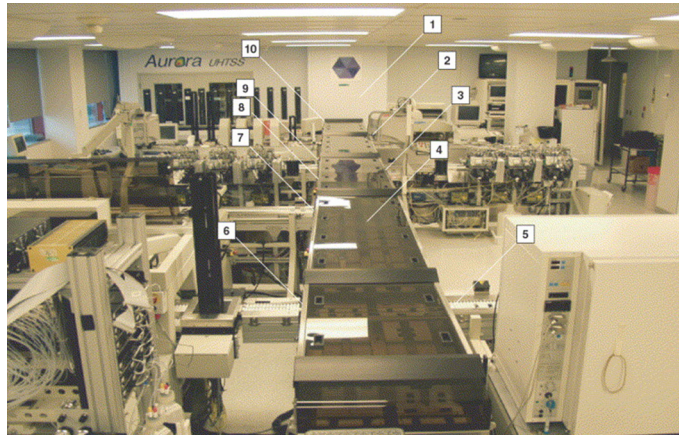


**FIGURE 2.17** The automated uHTS system at Bristol-Myers Squibb. Integral components and subsystems are shown; (1) Compound store, (2) Hit-picking robot, (3) 3456 reagent dispensing robot, (4) Transport, (5) Incubators, (6) Piezo-electric distribution robot, (7) Topology compensating plate reader, (8) 1536 reagent dispensing robot, (9) Automated plate replicating system, (10) High-capacity stacking system. *Source: Reprinted from Cacace, A.; Banks, M.; Spicer, T.; Civoli, F.; Watson, J. An ultra-HTS process for the identification of small molecule modulators of orphan G-protein-coupled receptors. Drug Discovery Today, 8 (17), 785–792, copyright 2003, with permission from Elsevier.*

While it is not clear exactly when and where automation technology merged with the field of drug discovery, it is clear that by the end of the twentieth century nearly all pharmaceutical companies had transitioned to high throughput screening methods. Initially, screening assays were performed in 96-well microplates (standardized by the Society for Biomolecular Screening and the American National Standards Institute), but the drive for increased efficiency and lower costs eventually lead to the development of 384-, 1536-, and even 3456-well plate technology (Figure 2.18). The miniaturization of screening technologies also spawned advances in micro-fluidics and signal detection methods, as the increased plate density required decreased solution volumes and smaller signal windows. A standard 96-deep well plate could hold up to 1.0 mL of fluid per well, while the