### Reduced Customization

Many companies have experienced too many problems with highly customized filling equipment; thus, standardization of filling machines has made a comeback. Standardization includes vendor selection, PLCs, human machine interfaces (HMI, touch screens), component transfer systems, filling method, and design of rapid access barrier systems (RABS) or isolator enclosures. Reduced customization has resulted in faster line fabrication, shorter factory acceptance testing (FAT), and reduced risk associated with startup, site acceptance testing (SAT), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). Also, to be expected, maintenance is simpler and there is reduced need for space parts.

### Integrated and Compact Lines

The pharmaceutical industry is moving toward single-sourced, integrated filling lines. The BOC Edwards production freeze-dryers and associated automatic loading and unloading systems are a good example. For low-to-intermediate production volumes, compact lines such as IMA's Modular Aseptic Compact System have been implemented that includes vial washing, depyrogenation oven, and filling machine integrated as one complete unit.

### Filling Machines for Integration with Barrier Isolators or Rapid Access Barrier Systems

Streamlined filling machines have been produced to fit precisely into these isolator systems to optimize airflow, aid in sterilant distribution, be ergonomic with the gloveports, facilitate removal of waste, and making it easier to remove the source of jams. Such filling machines are linear fillers with small widths. Vial transport systems to these isolator filling machines have been improved to allow complete exposure to sterilizing gases, typically vapor phase hydrogen peroxide. Electron beam tunnels are available to surface sterilize tubs of prefilled syringes directly feeding a syringe filler. Automated bag opening has been integrated upstream of these tunnels and automated tub lid removal downstream to provide greater separation of operators from the process.

### Higher Grade Vial Capping

Because of European Union requirements for Grade A air supply over capping operations, capping machines are available with RABS enclosures that target unidirectional downward airflow over the capping head, sorting bowl, and chute.

### Integration of External Vial Washing

Vial washing machines can be purchased to wash the vial exterior after filling to remove potent compounds on the exterior surface for added operator and user safety. Such machines aim water rinses so that the vial caps are not wetted and filtered compressed air is used to dry the vials. External vial washing also can help to remove cosmetic defects.

### Closed Vial Filling Systems

Aseptic Technologies developed the Crystal® Closed Vial Filling System (CVFS) where a ready-to-fill plastic (cyclo-olefin copolymer) vial and thermoplastic elastomer are molded in a Grade A clean room, assembled robotically, then gamma irradiated prior to delivery to the manufacturer. The specialized filling machine needle pierces the stopper, liquid is filled into the vial, the needle is withdrawn, and the piercing trace is laser resealed to restore closure integrity. A cap, designed to keep the stopper surface protected until use, is placed by snap fit. All these operations are conducted inside a CVFS that ensures Grade A environmental control. More discussion of this technology is presented in Chapter 23, page 360.

## REFERENCES

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