Table 25-2 Organization of United States and European Union Good Manufacturing Practice Regulations

United States (Food and Drug Administration)[a]	Europe (European Union)[b]
Resources	Resources
Organization and personnel	Personnel
Buildings and facilities	Premises and equipment
Equipment	
Methods and materials	Methods and materials
Control of components, containers and closures	Documentation
Production and process controls	Production
Packaging and labeling control	Quality control
Laboratory control	Contract manufacturing and analysis
Documentation and distribution	Quality management
Holding and distribution	Qualified persons
Records and reports	Complaints and product recall
Returned/salvaged drug products	Self-inspection

[a]United States: The Code of Federal Regulations, Title 21, Food and Drugs, Parts 210 and 211, cGMP in Manufacturing, Processing, Packing, or Holding of Drugs and Finished Pharmaceuticals.
[b]Europe: Volume 4 of "The rules governing medicinal products in the European Union" contains guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use laid down in Commission Directives 91/356/EEC, as amended by Directive 2003/94/EC, and 91/412/EEC respectively.

continued violations of these standards can be used to prosecute violators in courts of law. The World Health Organization (WHO) version of GMP is used by pharmaceutical regulators and the pharmaceutical industry in over 100 countries worldwide, primarily in the developing world. The European Union's GMP (EU-GMP) enforces more compliance requirements than the WHO GMP, as does FDA's version in the United States.

Both U.S. and E.U. GMP regulations are organized into three main sections (Table 25-2). Such an organization demonstrates to some extent what both regulatory groups especially emphasize. For example, the U.S. GMPs emphasize documentation a little more than the European GMPs while Europe emphasizes Quality Management. However, as time has passed, requirements for GMP compliance have merged to essentially the same emphasis regardless of manufacturing location.

Because GMP regulations were first proposed in 1963 and enacted as law in 1978 with relatively minor changes, it is important to consider the "c" in cGMP. GMPs are *current*, which means that the meaning and application of GMPs change as the industry changes. Four main areas of change in the industry include the following:

1. Scientific and technological advances—Examples include computer systems, computer process control, paperless manufacturing, electronic signatures, barrier isolation technologies, biotechnology medicine manufacturing, and many other examples.
2. Adverse events—Examples include product tampering incidents, product recalls caused by lack of understanding or lack of control of processes, contamination incidents, and needle safety precautions.
3. Inspection activities and findings—Examples include the generic drug scandal of the late 1980s, lack of GMP compliance in manufacturing of active pharmaceutical ingredients, dealing with out-of-specification data, poor documentation practices, lack of aseptic process validation and many other validation studies, and many of other examples.
4. Industry practice—Examples include introduction of laboratory management systems, improvements in all aspects of manufacturing (equipment advances, automation, inspection, etc.), new drug delivery systems (e.g., micro-and nano technologies), new analytical methods, and many other examples.

Interpretation and application of cGMPs have had to adjust and adapt to all these sources of change over the years. Often, this has led to confusion and controversy that has taken months to years to resolve. Undoubtedly, changes will always be the rule rather than the exception so cGMPs will always evolve over time.