addition to phosphate buffers, glycinate, carbonate, and citrate buffers can be used, in which case, sodium, potassium, or ammonium ions can serve as a counterion.

Lyoprotectants include molecules, which, when combined with a protein of interest, prevent or reduce chemical and/or physical instability of the protein upon lyophilization and subsequent storage. Preservatives include an agent that reduces bacterial action and that may be optionally added to the formulations herein. The addition of a preservative may, for example, facilitate the production of a multiuse (multiple-dose) formulation. Examples of potential preservatives include octadecyldimethylbenzyl ammonium chloride, hexamethonium chloride, benzalkonium chloride (a mixture of alkyl benzyl dimethylammonium chlorides in which the alkyl groups are long-chain compounds), and benzethonium chloride. Other types of preservatives include aromatic alcohols such as phenol, butyl, and benzyl alcohol, alkyl parabens such as methyl or propyl paraben, catechol, resorcinol, cyclohexanol, 3-pentanol, and m-cresol.

Surfactants are surface-active molecules containing both a hydrophobic portion (e.g., alkyl chain) and a hydrophilic portion (e.g., carboxyl and carboxylate groups). The surfactant may be added to the formulations of the invention. Surfactants suitable for use in the formulations of the present invention include, but are not limited to, polysorbates (e.g., polysorbates 20 or 80); poloxamers (e.g., poloxamer 188); sorbitan esters and derivatives; Triton; sodium lauryl sulfate; sodium octyl glycoside; lauryl, myristyl, linoleyl, or stearyl sulfobetadine; lauryl, linoleyl, or stearyl sarcosine; linoleyl, myristyl, or cetyl betaine; lauramidopropyl, cocamidopropyl, linoleamidopropyl, myristamidopropyl, palmidopropyl, or isostearamidopropyl betaine (e.g., lauroamidopropyl); myristamidopropyl, palmidopropyl, or isostearamidopropyl dimethylamine; sodium methyl cocoyl or disodium methyl oleyl taurate; and the MONAQUAT™ series (Mona Industries, Inc., Paterson, NJ), PEG, polypropyl glycol, and copolymers of ethylene and propylene glycol (e.g., Pluronics, PF68).

The principles governing protein solubility are more complicated than those for synthetic small molecules, thus overcoming the protein solubility issue takes different strategies. Operationally, solubility for proteins could be described by the maximum amount of protein in the presence of cosolutes whereby the solution remains visibly clear (i.e., does not show protein precipitates, crystals, or gels). The dependence of protein solubility on ionic strength, salt form, pH, temperature, and certain excipients is well demonstrated by changes in bulk water surface tension and protein binding to water and ions versus self-association. The binding of proteins to specific excipients or salts influences solubility through changes in protein conformation or masking of certain amino acids involved in self-interaction. Proteins are also preferentially hydrated (and stabilized as more compact conformations) by certain salts, amino acids, and sugars, leading to their altered solubility.