understand the most probable degradation pathways associated with the candidate, and assess the appropriate accelerated conditions to utilize during screening. Real-time stability, although preferred, is time consuming early in programs to utilize for screening.

Due to the route of administration associated with vaccines, mainly parenteral, the formulation scientist is also challenged with a limited range of excipients that are available for use [25–27]. Although generally regarded as safe (GRAS) excipients are examined across TPs, pharmaceuticals, and vaccines, the list is significantly constrained for injectable products (Table 2). Additionally, as the global markets for vaccines expand, animal-derived raw materials and excipients must be removed to satisfy regulatory requirements in many markets such as China and Japan.

The range of vaccines and the stability issues associated with them are quite variable. Vaccines can be as diverse as live-attenuated or inactivated viruses, polysaccharides or polysaccharide conjugates, subunit/peptide vaccines consisting of native or recombinant proteins, and unadjuvanted or adjuvanted vaccines [28]. This adds additional layers of complexity to the formulation scientist since there are not "platform" formulations or technologies that can be utilized to support the different vaccine candidates. In addition, the assays required to monitor the stability and degradation pathways vary significantly from vaccine product to product.

Since the variability in vaccine candidates is vast, the formulation scientist relies substantially on their analytical colleagues to establish stability-indicating assays that can shape the final drug product process and formulation. From an analytical perspective, vaccines can be significantly challenging. The methods being developed in many cases must be able to distinguish differences for each individual antigen associated with the multicomponent vaccines. The large size of vaccines (>10,000-fold larger than a pharmaceutical) and low concentrations of the active

Table 2 Common excipients in vaccine drug product development and expected impact in product

Excipient	Common examples	Impact in formulation
Salts	Ammonium sulfate, calcium chloride, sodium chloride, magnesium chloride, potassium chloride	Tonicity modifier
Buffers	Succinate, sodium phosphate, potassium phosphate, histidine, hepes, tris	pH
Sugars and polyols	Cyclodextrin, sucrose, sorbitol, trehalose, lactose, glycerol, mannitol	Stabilizing effect
Amino acids	Arginine, proline, glycine, glutamic acid, aspartic acid	Stabilizing effect, aggregation modifiers, bulking agents
Surfactants	Poloxamer 188/407, polysorbate 20/80, sodium lauryl sulfate	Air surface interfaces, mitigation of surface adsorption
Antioxidants	Ascorbic acid, glutathione, methionine	Prevention of oxidation
Polymers	Dextran, polyethylene glycol	Bulking agents, freeze-point depressors
Preservatives	M-cresol, phenol, 2-phenoxyethanol, chlorobutanol, methylparabens	Antimicrobials