(BCG) and the small pox vaccine were formulated as multidose dried powders. "DryVax" small pox vaccine was launched in the 1940s for mass immunization in several countries [25–27]. This was one of the first commercial launches of a sterile dry formulation for parenteral use. The 100-dose single-vial composition also contained phenol as a preservative. DryVax was manufactured by Wyeth Laboratories until the early 1980s and manufactured by Aventis Pasteur (now Sanofi) and is no longer licensed in the USA; it revoked in 2008 [25–27].

Leslie Collier is credited with helping develop a viable vaccine that led to the eradication of smallpox. Collier's major contribution was in perfecting the art of freeze-drying method of producing the vaccine for mass use (Leslie H. Collier, b. 1921). As a graduate student at the Lister Institute of Preventive Medicine, Elstree, Hertfordshire, England, in the early 1950s, Dr. Collier developed the method of freeze-drying of vaccinia virus that was subsequently adapted to large-scale freeze-dried vaccine production in many laboratories throughout the world [28, 29].

This was a very critical step in making the vaccine available for mass distribution, as earlier vaccine required refrigeration. The original method of freeze-drying of a small pox vaccine employed by Camus and others was suboptimal. Phenol was added to the freeze-dried vaccine as an antimicrobial agent. Despite its effectiveness as an antimicrobial agent, phenol also damaged the virus. This opened the door for researchers looking for an alternative excipient to add to the composition for a longer shelf life. Collier added a key component "peptone" to the process of freeze-drying. The powder was reconstituted with a solution of glycerin [28, 29]. This modified freeze-drying process to a large extent was the main driver in leading to global eradication of small pox. Similar efforts in Europe were also demonstrated effectively with a BCG freeze-dried composition. This further led to the acceptance of BCG vaccination in endemic countries very quickly. Most of these freeze-dried vaccines were distributed through governmental agencies around the world. This also enabled the reduction in the cost of goods as some of these were formulated in multidose vials for broader population coverage [30–38].

Despite the success with small pox and BCG, most toxoids and adjuvants used from 1930 onwards did not succeed in being freeze-dried. The primary reason attributed to their failure was adsorption on mineral salts. Aluminum hydroxide and aluminum phosphate, the two primary salts used for adsorption with diphtheria and tetanus toxoid, were not compatible with the dehydration approach as significant aggregation of the mineral salts was seen upon freezing and the loss of potency in vivo of toxoids upon freezing was observed [30–36].

Another vaccine that has made a major impact on providing postexposure protection in endemic countries using a freeze-dried vaccine, is the rabies vaccine. A freeze-dried rabies vaccine was developed in the 1960s that led to a longer shelf life and aided in better utilization in a postexposure setting in developing countries. To this date, in many developing countries, a freeze-dried rabies vaccine is used after reconstitution by the intramuscular route and also in smaller volumes of 100 μl through the intradermal route. Some of the licensed freeze-dried rabies vaccines on the market are RabAvert and Rabipur [34–38].