Adjuvants: Introduction

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Traditional vaccines derived from **live-attenuated-** or **inactivated whole organisms** or **toxins** were effective in inducing predominantly antibody-based immunity, but highly **reactogenic**. Developments to produce safer, less reactogenic vaccines also capable of inducing cell-mediated immunity have resulted in compromised vaccine efficacy. **Adjuvants** (taken from the Latin, "adjuvare," meaning "to help") are designed to improve poorly immunogenic vaccines. Adjuvants were originally described by Ramon as *'substances used in combination with a specific antigen that produced a more robust immune response than the antigen alone,'* thus encompassing a wide range of materials.

Adjuvants affect the immune response in various ways:

- To increase the immunogenicity of weak antigens
- To enhance speed and duration of immune response
- To stimulate and modulate humoral responses, including antibody isotype
- To stimulate cell-mediated immunity
- To improve induction of mucosal immunity
- Enhance immune responses in immunologically immature patients, particularly infants
- To decrease the dose of antigen required; reducing costs and eliminating inconvenient requirements for booster shots

Many molecules have been considered for use as an adjuvant, including mineral compounds (e.g. Alum), water-in-oil or oil-in-water emulsions (e.g. Freund's adjuvant), as well as natural and synthetic toxins derived from bacteria (e.g. cholera toxin, CT and lymphotoxin, LT). Based on their mechanism of action, adjuvants have been categorised into two broad groups; the **particulate vaccine-delivery systems** that target antigen to **antigen presenting cells** (**APCs**) and the **immunostimulatory adjuvants** that directly activate such cells through specific receptors e.g. **toll-like receptors** (**TLRs**) resulting in inflammatory responses that amplify the innate immune response. The ultimate aim is to activate the innate immune system to respond more rapidly to infection and for the adaptive immune response to become more specific.

The precise mechanisms of many adjuvants remain largely undefined due to the complexity of the immune response, but generalisations can be made to allow the design of more rational adjuvants aimed at particular arms of the immune system.

Summary of adjuvants approved for human use

Adjuvant	Description	Approved vaccine products
Aluminium-based mineral salts (Alum)	E.g. Aluminium phosphate, Calcium phosphate, Aluminium hydroxide	Eg. Anthrax (BioThrax®, Emergent Biosolutions) Hepatitis A (Vaqta®, Merck) DTP (Triple Antigen™, CSL limited)
MF59	Submicron oil-in-water emulsion	Influenza (FLUAD®, Novartis)
Monophosphoryl lipid A (MPL)	Bacteria-derived immunostimulant	Hepatitis B (Fendrix®, GlaxoSmithKline)
Virosomes	Spherical vesicles containing viral membrane proteins in the lipid membrane	Hepatitis A (Epaxal®, Berna Biotech) Influenza (Inflexal®, Berna Biotech)