Vaccine Adjuvant Technology

By Croda

Smart Science to Improve Lives™

CRODA

Agenda

Introducing Croda and our Health Care Business

Vaccine Adjuvant Expertise

Vaccine Adjuvant Portfolio & Pipeline

Who We Are

Since 1925, we have been the name behind the high performance ingredients and technologies in some of the biggest, most successful brands in the world: creating, making and selling speciality chemical ingredients that are relied on by industries and consumers everywhere.

Science

Innovation

Together

Everywhere

Energetic

Evolving

Influence

Responsible

Flexible

Our Business Areas

Personal Care

Life Sciences

Performance Technologies

Industrial Chemicals

Crop Care

Health Care

Crop Protection

Seed Enhancement

Biostimulants

Vaccine Adjuvants

High Purity Excipients

Omega 3 API

incotec

plantimpact

BRENNTAG Biosector

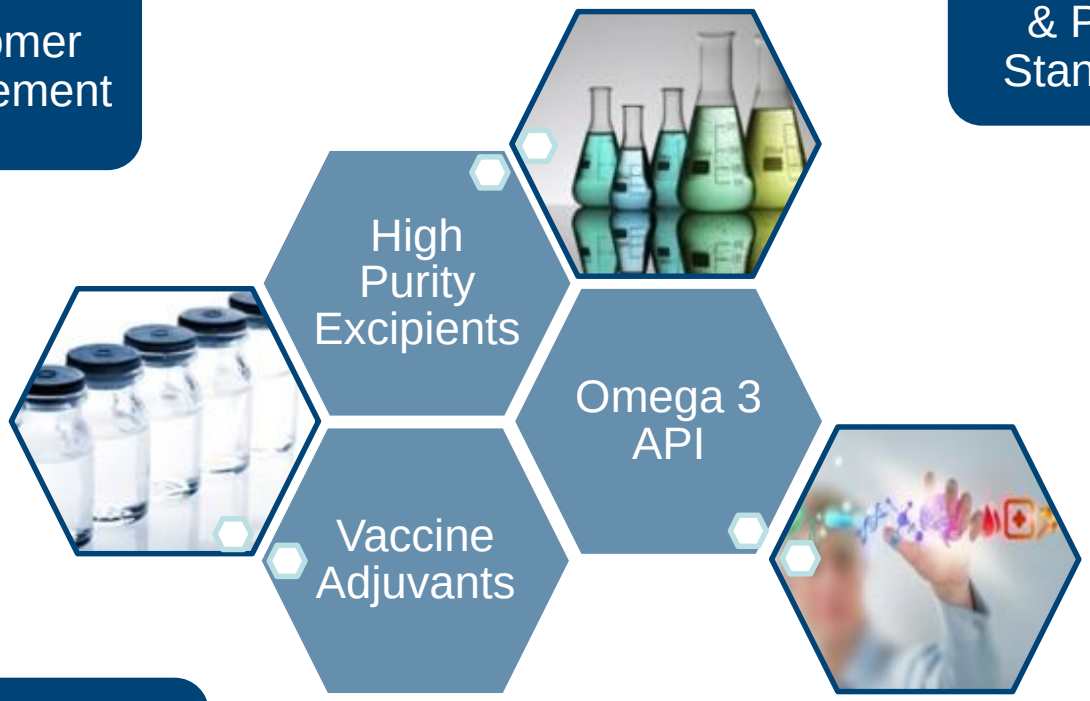
sisaf

enza biotech

What Distinguishes Us

Customer Engagement

High Quality & Purity Standards



Regulatory Expertise

Strong Customer Service

Continuous Innovation

Dedication and Commitment

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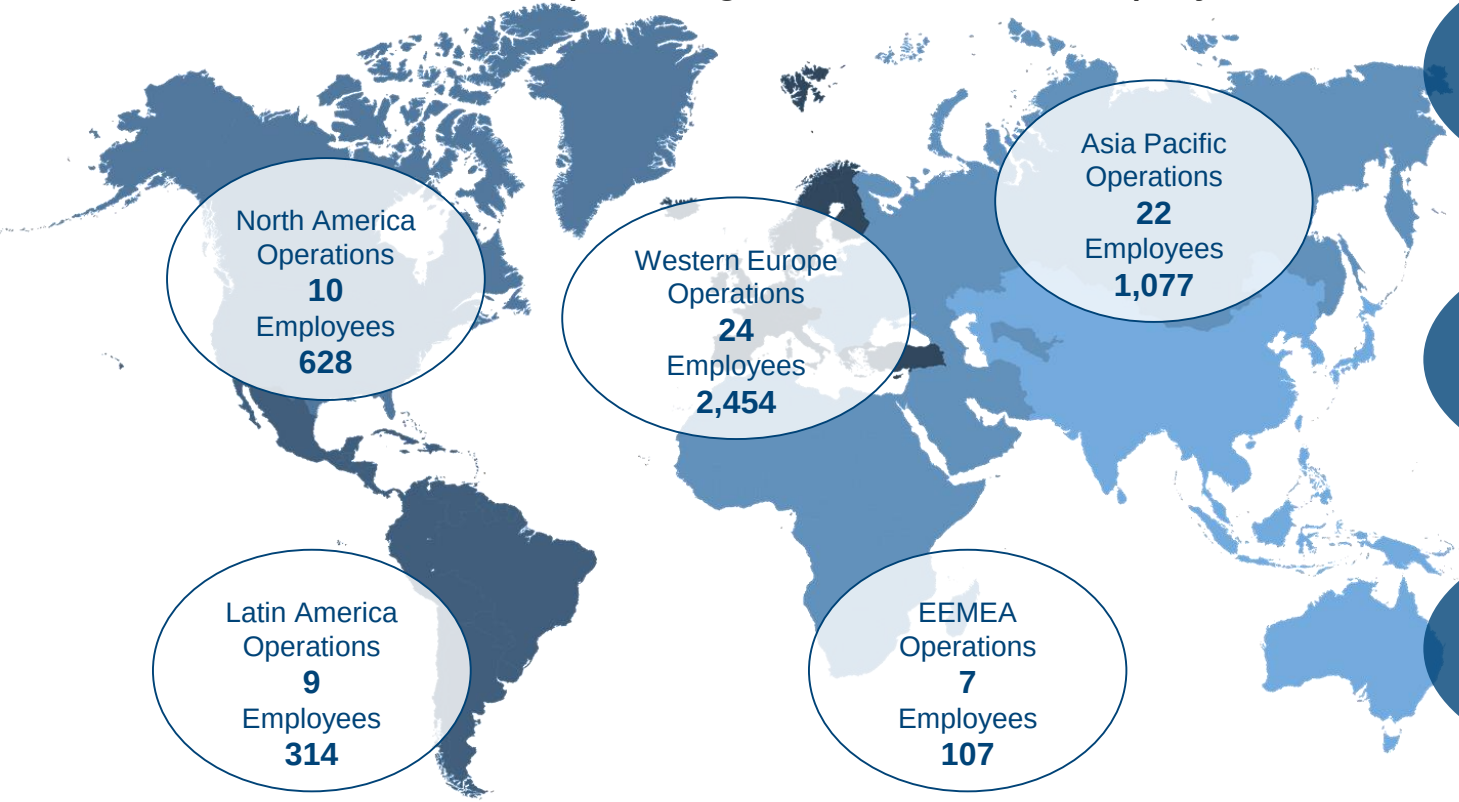
Where We Operate

Our global network at your service

38 Countries 72 Operating Sites 4,580 Employees

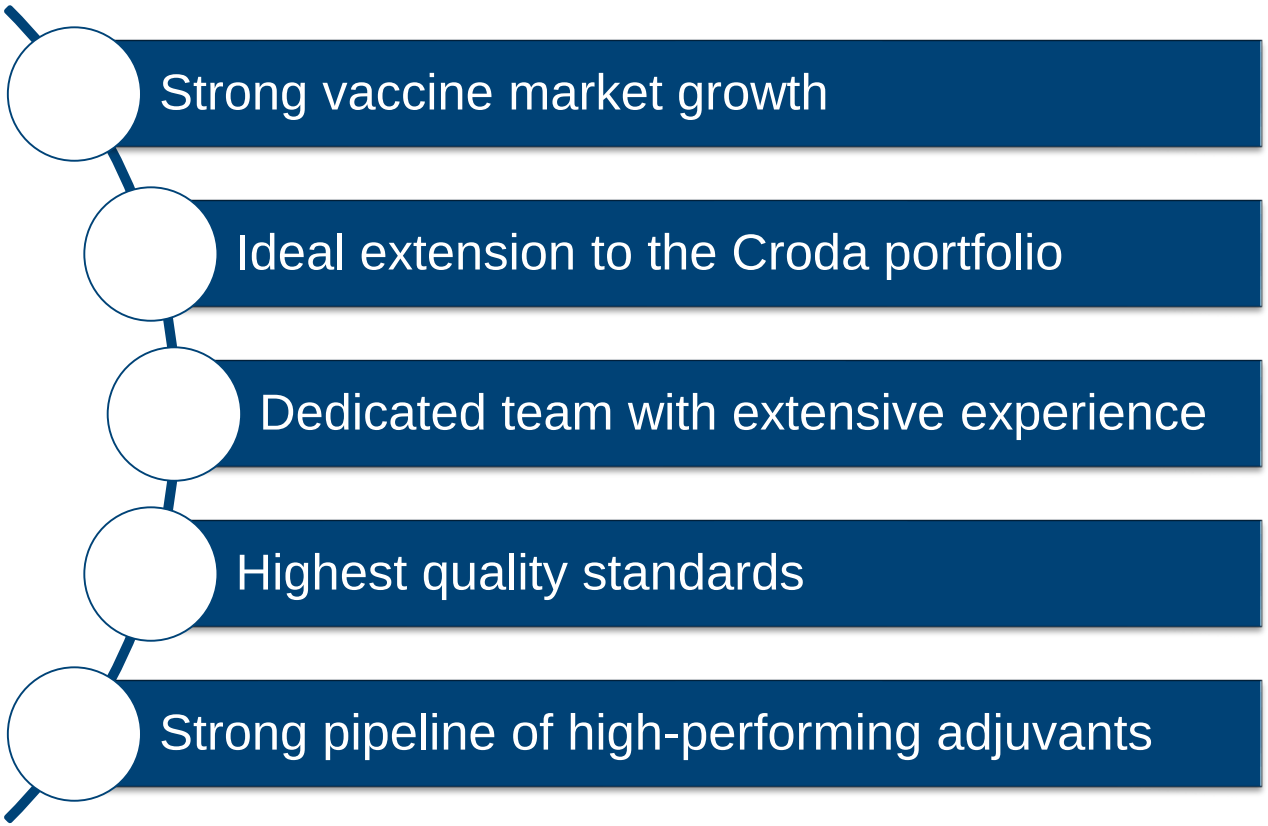


Global Organisation
Core to Croda

Multi-Region R&D
Diverse Perspectives

Secure Supply
Multiple manufacturing sites, local stock and service

Acquisition Rationale



Croda's Vision for Vaccine Adjuvants

Be recognised as an adjuvant powerhouse

Strengthen customer relationships

Grow global sales via Croda's network

Stronger Together: broader market insight

Stronger Together: enhanced R&D pipeline

Selective investment to drive future growth

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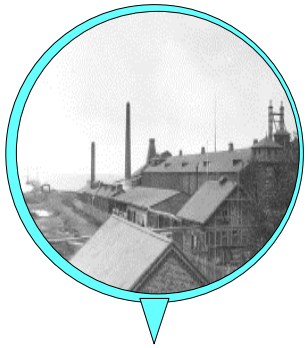
Proven History in Vaccine Adjuvants

First Superfos Adjuvant Plant



1939

1990

Site in Frederikssund opened

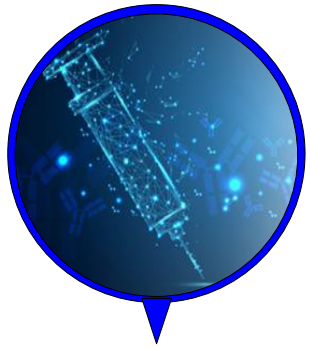
Brenntag Biosector established

2001

2012

Plant Expansion

Croda acquires Brenntag Biosector and its vaccine adjuvant portfolio



2018

Industry Leading Site Credentials

- Croda Denmark has the highest quality standards, running the only aseptic manufacturing site for vaccine adjuvants globally

- The widely recognised adjuvants Adju-Phos and Alhydrogel are sterilised and aseptically filled

- The site is continuously working to met cGMP and increasing regulatory requirements in the human and veterinary industry


LÆGEMIDDELSTYRELSEN
DANISH MEDICINES AGENCY

Tilladelse til fremstilling og indførsel af lægemidler og mellemprodukter
Manufacturing and Importation Authorisation

- Croda Denmark is a Holder of Manufacturing and Importation Authorisation (MIA) for medicines and intermediate products in accordance with The Danish Medicines Act § 39 and EU GMP Part I

Production

Centrifuge suites

Ultrafiltration

Ultrafiltration and freeze drying

Clean Rooms – Grade B/C/D

Aseptic Production

Striving towards the
highest quality and safety

Industry Leading Expertise

Peter Holm Tygesen – Managing Director Vaccine Adjuvants

- More than 25 years of pharmaceutical management experience
- More than 13 years with Lundbeck in different positions in R&D and production management
- CEO of the Biotech company Egalet and Riemann
- Excels in driving change management and in interacting with partners and authorities

Dr. Erik B. Lindblad – R&D Director Vaccine Adjuvants

- Internationally renowned vaccine adjuvant expert
- Authored numerous scientific publications
- More than 30 years of experience with vaccine adjuvants
- Responsible for designing and establishing the Frederikssund/Denmark site in 1990

Jette Kjeldal –Quality & Regulatory Director Vaccine Adjuvants

- Long experience with development, production and quality assurance under Good Manufacturing Practise (GMP) for sterile APIs, sterile and non-sterile medicinal products (EU GMP Part I and II) and medicinal devices for in vitro diagnostics (ISO13485)
- Extensive knowledge about quality systems and processes, drug master filings and other regulatory activities

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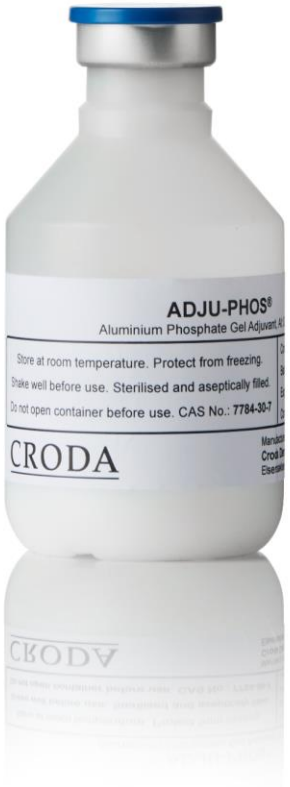
Industry Leading Products

- Alhydrogel®
- Adju-Phos®
- Quil-A®
- QS-21



Alhydrogel®

Benefits

- Best studied aluminium adjuvant product in the world
- 80 years history of safe and effective use in commercial vaccines
- EU GMP certified production of aseptically prepared sterile products (Part I: Medicinal Products for Human and Veterinary Use)
  - Manufactured in classified clean rooms
  - Sterilised and aseptically filled in a grade A clean room
- Low levels of metals (Cu, Ni, Fe) help ensuring antigen stability

Applications

- Human and veterinary vaccines
- Blood plasma fractionation

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Alhydrogel®

Features

- Very low conductivity resulting in a buffer dependent binding capacity
- Positive charge at neutral pH
- Effectively adsorbs negatively charged antigens
- Boosts antibody-mediated (Th2) response
- Can be combined with other adjuvants (such as Monophosphoryl Lipid) to achieve a balanced Th1/Th2 immune response

Available concentrations

- Alhydrogel 1.3%
- Alhydrogel 2%
- Alhydrogel ”85” (approx. 20% higher protein adsorption capacity)

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Adju-Phos®

Benefits

- Best studied aluminium phosphate adjuvant
- More than 40 years history of safe and effective use in commercial vaccines
- EU GMP certified production of aseptically prepared sterile products (Part I: Medicinal Products for Human and Veterinary Use)
  - Manufactured in classified clean rooms
  - Sterilised and aseptically filled in a grade A clean room

Applications

- Human vaccines
- Veterinary vaccines

Vaccine Adjuvants

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Adju-Phos®

Features

- Negative charge at neutral pH
- Effectively adsorbs positively charged antigens
- Boosts antibody-mediated (Th2) response
- Can be combined with other adjuvants (such as Monophosphoryl Lipid) to achieve a balanced Th1/Th2 immune response

Available variants

- Adju-Phos pH ~ 6.5
- Adju-Phos pH ~ 5.0

Both variants contain 0.9% NaCl to reduce injection site discomfort

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Quil-A®

Benefits

- Highly concentrated and potent saponin adjuvant purified from bark extract of the Quillaja saponaria Molina tree
- More than 35 years of safe and effective use in commercial vaccines
- Adjuvant efficacy verified by vaccine tests for each raw material batch
- EU GMP certified production (Part I: Medicinal Products for Human and Veterinary Use)
  - Sterile filtered prior to lyophilisation to ensure a low bioburden and long shelf life period

Applications

- Veterinary vaccines
- Active component of ISCOM and nanoparticle adjuvants

Vaccine Adjuvants

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Quil-A®

Features

- Potent activation of dendritic cells and induction of cytokines/chemokines
- Stimulates both the cell-mediated (Th1) and the antibody-mediated (Th2) immune response to antigens
- Potential to combat a wide range of bacterial and viral pathogens
- Cost-effective due to very low dose

Available variants

- Supplied as a water-soluble lyophilised powder with minimum 95% dry matter
- Also available with the antioxidant ascorbic acid which may improve stability of aqueous solutions of the product

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Vaccine Adjuvants

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QS-21

Features

- Purified triterpenoid saponin molecule fraction from the bark of the South American tree Quillaja saponaria
- Kensil et al isolated QS-21 in 1991 and demonstrated an optimal balance of high immunostimulation and tolerable reactogenicity
- QS-21 exerts well-balanced Th1 and Th2 immune response, it stimulates both the innate and humoral immune system
- Outperforms other classes of adjuvants and suitable for use in human vaccines
- Since October 2017, QS-21 is a component of a FDA approved licensed vaccine against herpes zoster and post-herpetic neuralgia (Shingrix)

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Exciting Projects In Our Pipeline

There is a growing need for new and efficacious adjuvant systems. The current pipeline includes:

- Adju-Phos ZP
  - A new Adju-Phos product variant with phytic acid
  - Reduced particle size, increased ζ–potential ie higher binding capacity
  - Interesting in multivalent vaccines and for antigen sparing
- NanoQuil
  - Proprietary saponin-based technology platform

Vaccine Adjuvants

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Adju-Phos® ZP

Features

- Modified surface characteristics to enhance ζ-potential and reduce the size of the gel particles
- Enables higher adsorption of protein antigen (positively charged protein antigens with alkaline isoelectric point)
- Potentially more balanced Th1/Th2 immune response
- Potential for multivalent vaccines
  - More antigens in the same vaccine, eg more antigens in existing pentavalent vaccines
  - Development of new multivalent aluminium phosphate based vaccines
- Simplified vaccination campaigns
  - Fewer vaccinations
  - Improved patient compliance
  - Advantages for remote vaccination in developing countries

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Adju-Phos® ZP Status

- Process developed and proof of concept established
- Patent application published on October 24, 2019
- Samples available for research purposes

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NanoQuil®

Features

- Precision adjuvant platform for preventive and therapeutic vaccines
- NanoQuil can prevent both viral and bacterial infections (stimulates Th1 and Th2 reponses)
- NanoQuil are nanoparticles of cholesterol and Quillaja saponin (w/wo stevia) with flexibility in design and manufacture (customisation)
- NanoQuil may be tuned and adapted to various antigens for optimal efficacy
- NanoQuil is protected by strong IP (multiple patents)

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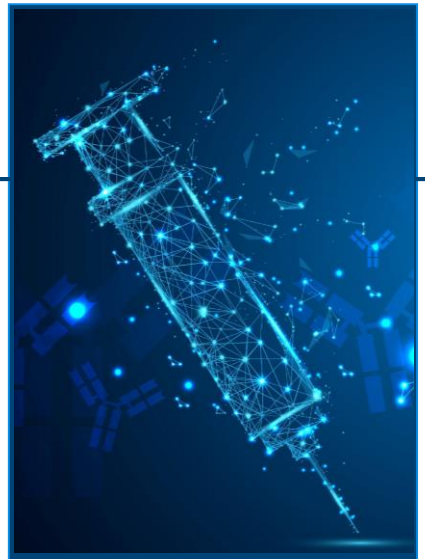
Summary

- The vaccine adjuvants from former Brenntag Biosector are a highly valuable and future-looking addition to Croda's product offer
- They are manufactured according to highest quality standards in the only aseptic manufacturing site for vaccine adjuvants worldwide
- The portfolio includes market-leading well-known brands such as Alhydrogel and Adju-Phos and technically advanced saponin-based adjuvant systems
- A rich development pipeline demonstrates the innovation capacity of the highly experienced and dedicated team of experts
- Croda's dedicated global sales network will contribute to satisfy growing demand for new and efficacious adjuvant systems



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Thank you!

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