# PRODUCTION OF NANOEMULSION ADJUVANTS USING HIGH SHEAR FLUID PROCESSING


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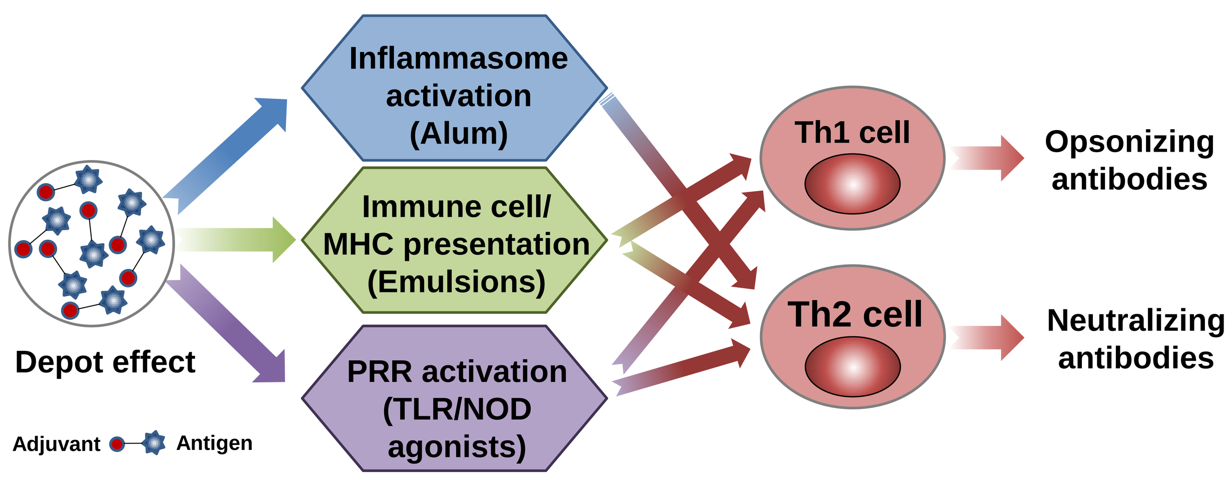
## Introduction

### Vaccine Adjuvants

- Vaccine adjuvants enhance the efficacy of vaccines.
- Most new adjuvants are emulsions or liposomes with particle sizes below 200 nm.
  - Effective: Enhance both Th1, Th2 and MHC responses[1,2]
  - Well tolerable
  - Biodegradable

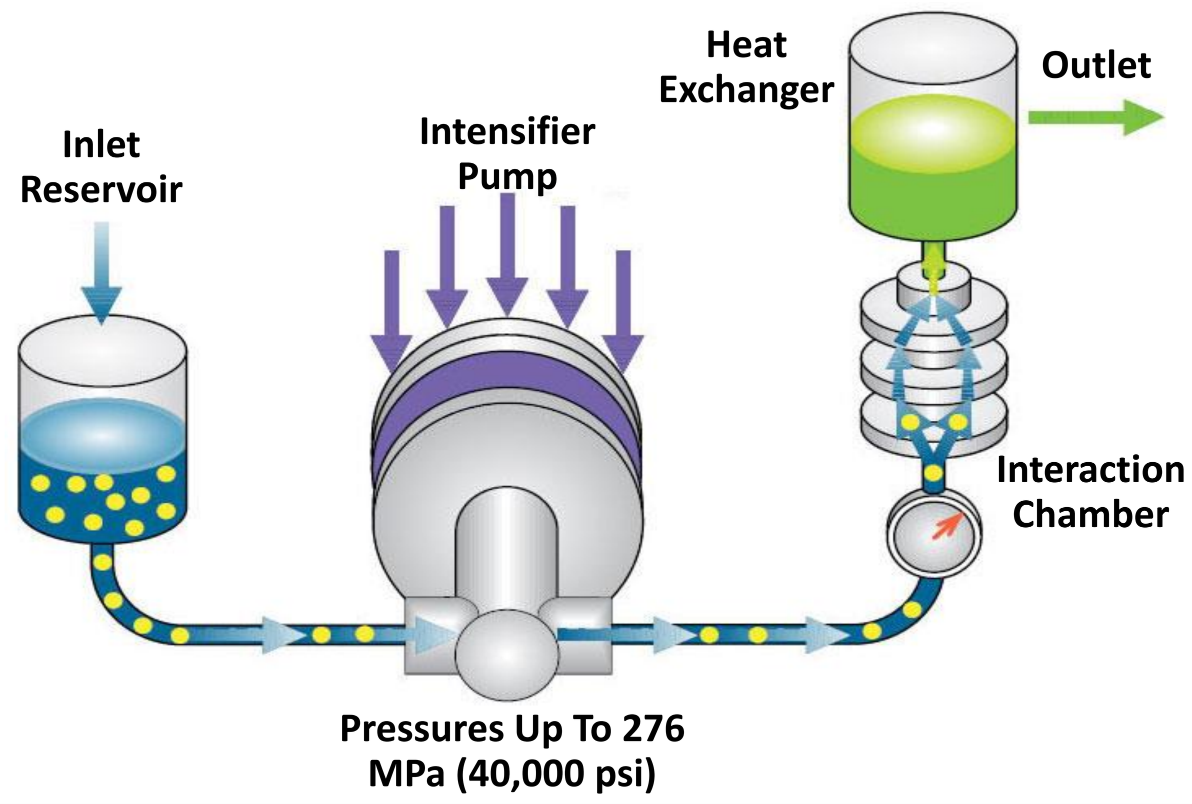



### Key Production Requirements & Challenges

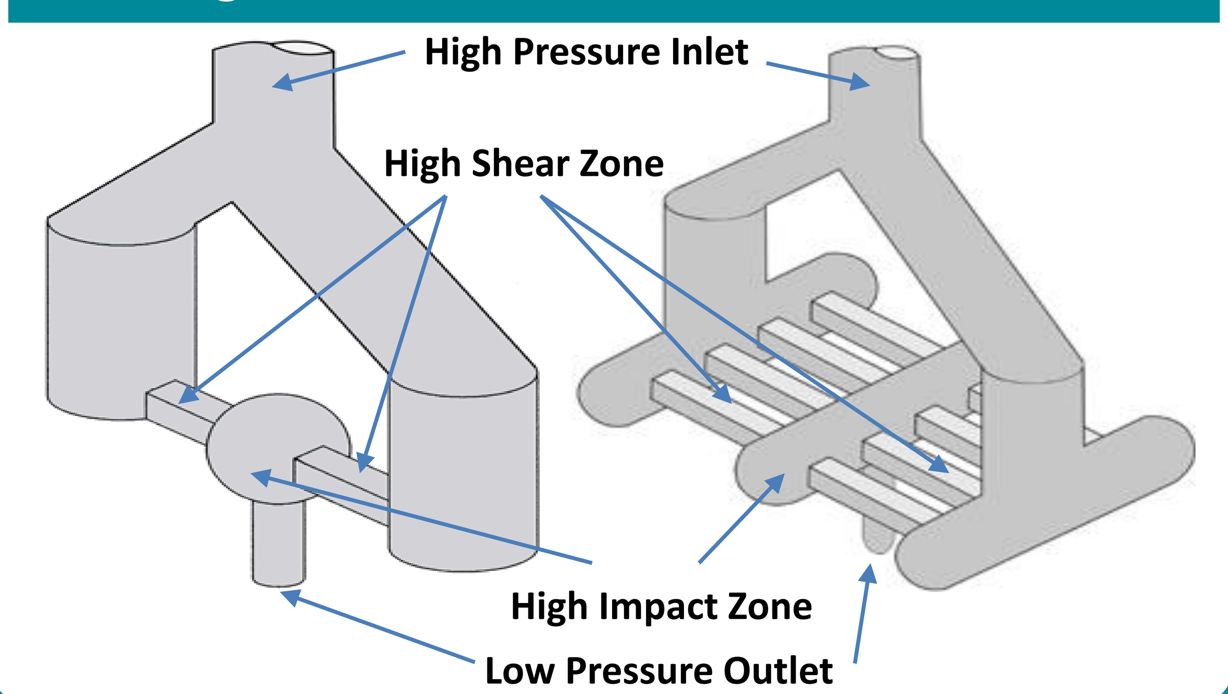
- Process efficiency.
- Sterile production.
- Repeatability & scalability.

### Microfluidizer® Technology

- High pressure is used to pump multi-phase fluids through the microchannels of an interaction chamber, exposing the fluids to high shear.
- Velocities of over 400 m/s in micron channels result in shear rates of up to $10^8$ $s^{-1}$.
- Parallel arrays of identical microchannels ensure linear scalability to tens of liters per minute.



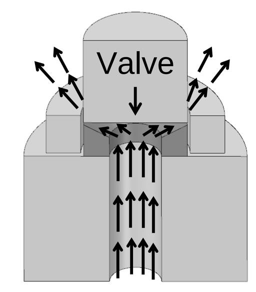

**"Y" Single-Slotted** **"Y" Multi-Slotted**



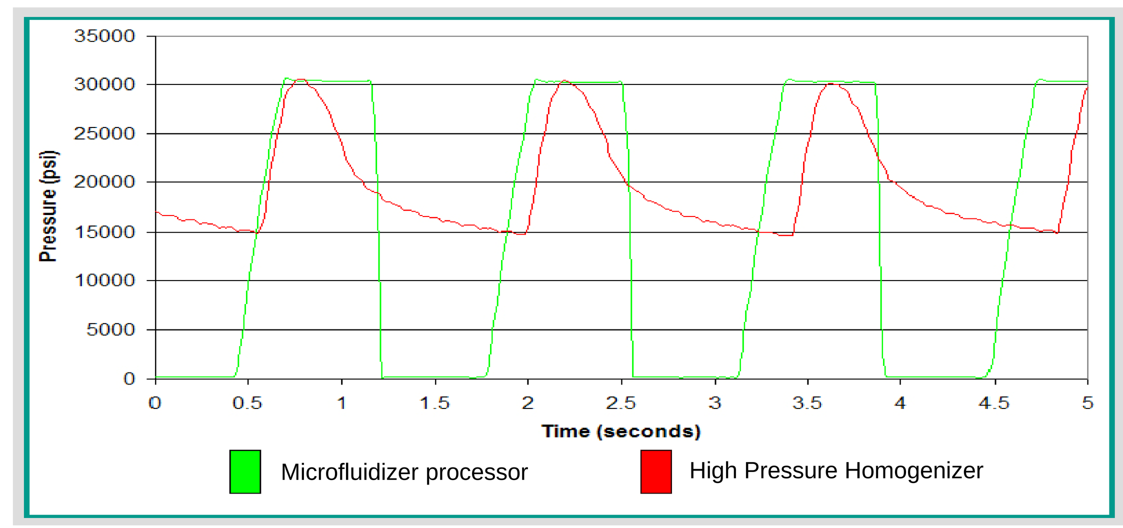

## Case Study

### Production of Squalene Nanoemulsion Adjuvant

- Microfluidizer® technology:
  - Fixed geometry interaction chamber
  - Constant pressure profile
- High pressure homogenization:
  - Variable geometry valve
  - Dynamic pressure profile
  - Constant volume




### Pressure Profile

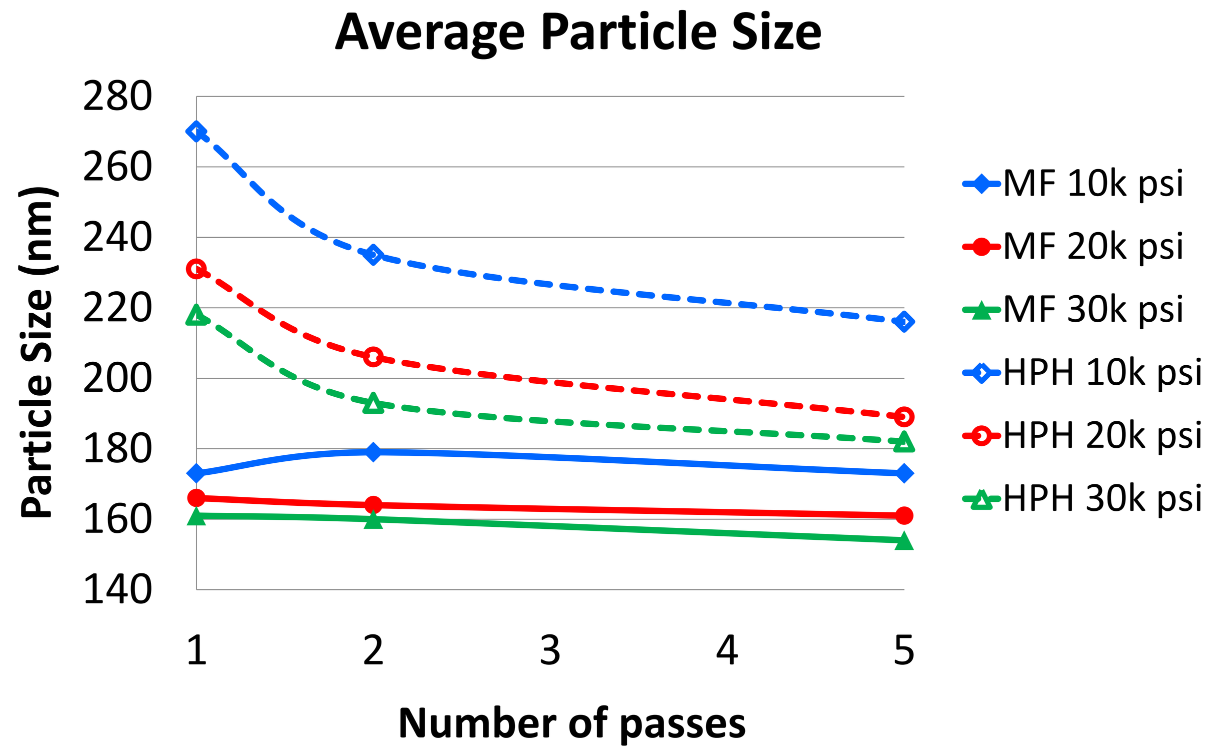



### Method

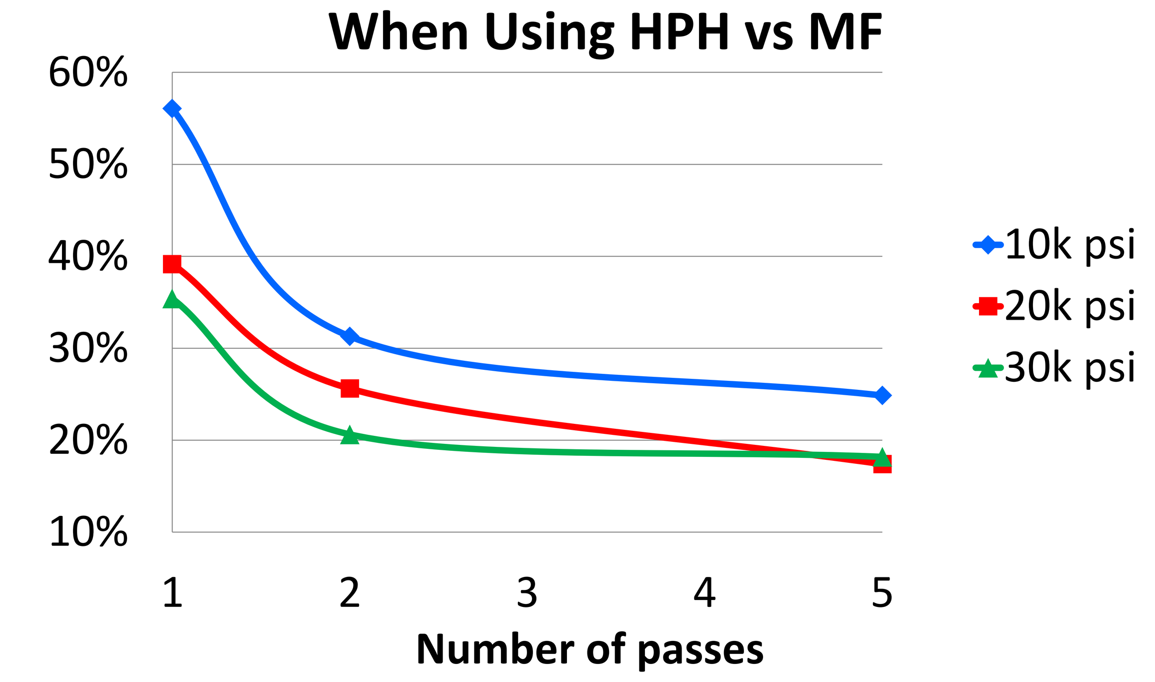
- Oil-in-water emulsion formulation with 4 wt% squalene oil and 1 wt% surfactant.
- Pre-emulsion was prepared using a rotor-stator mixer (Quadro HV0).
- Parameters varied during processing: pressure and number of passes through the processer.
- Particle size analyzed using a dynamic light scattering instrument (Malvern Zetasizer Nano-S).

## Results

### Average Particle Size




### Percent Increase in Average Particle Size When Using HPH vs MF



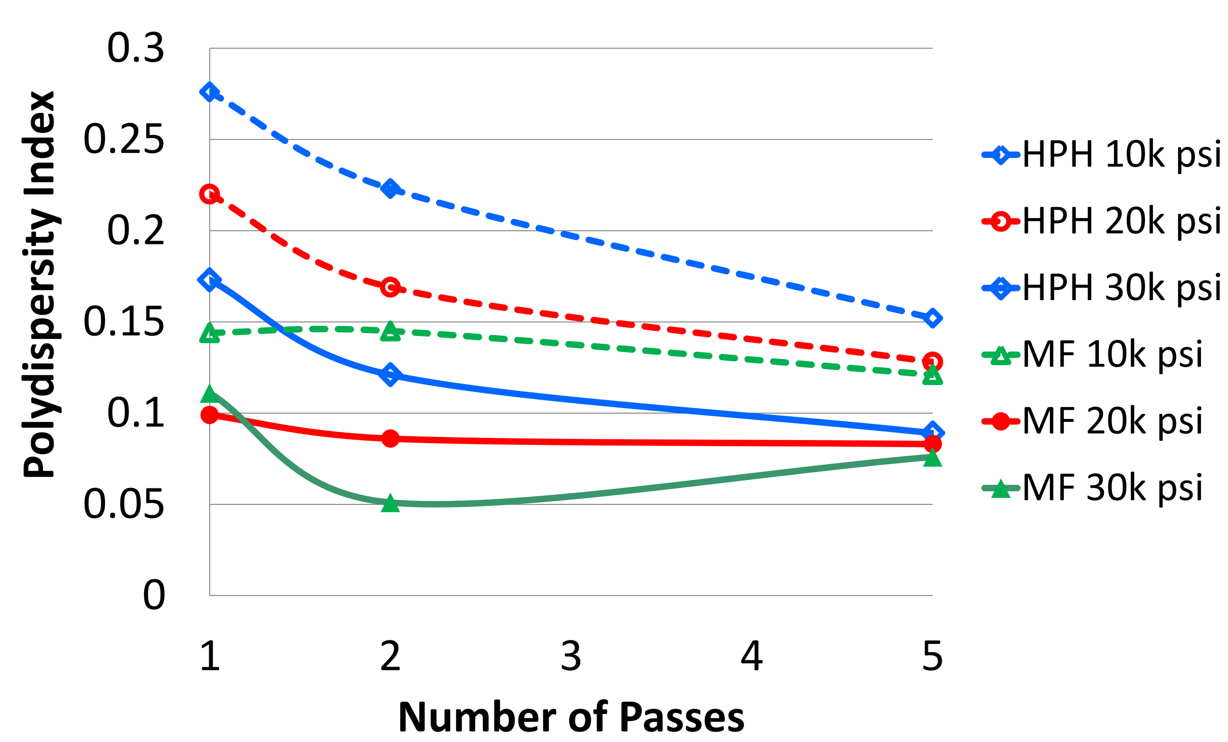

### Power Consumption to Achieve A Particle Size at A Given Flow Rate

- Power = Pressure x Number of Passes x Flow Rate

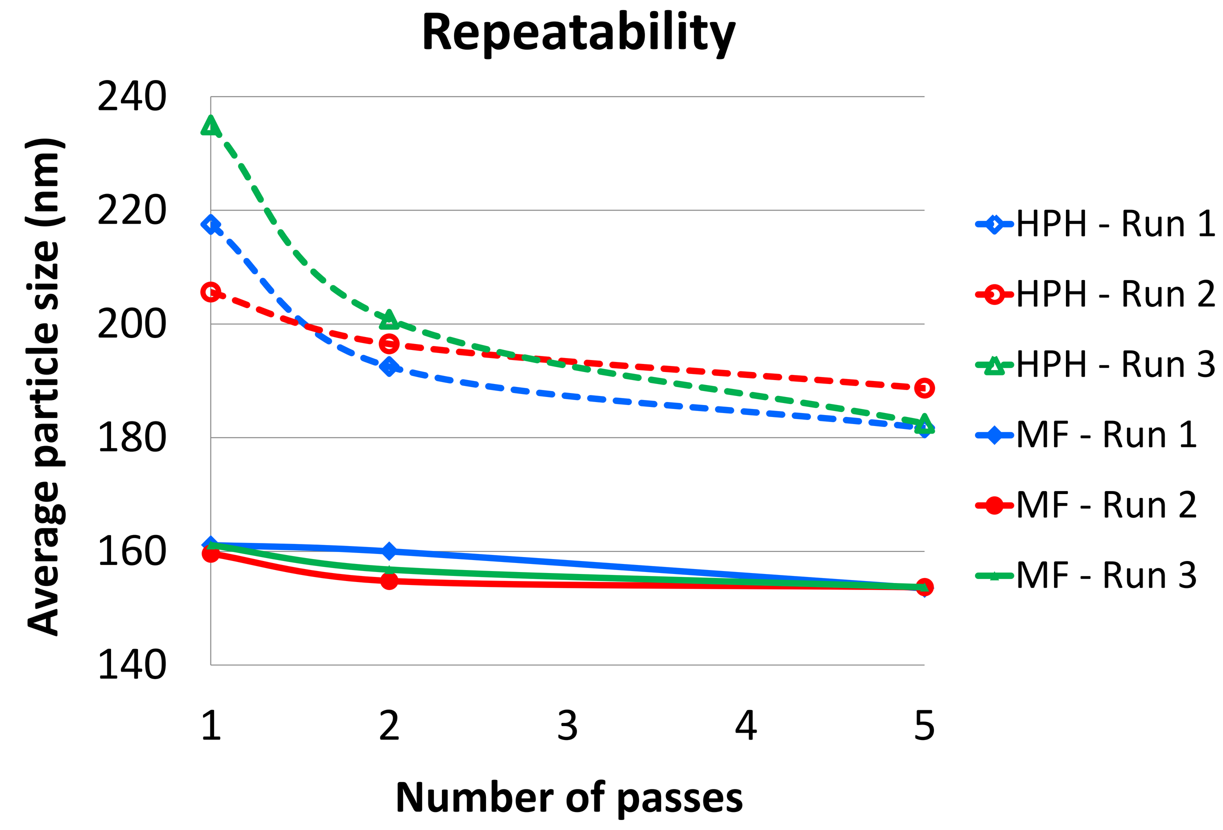
| | Particle Size (nm) | Process Pressure (psi) | Number of Passes |
|---|---|---|---|
| Homogenizer | 178 | 30,000 | 5 |
| Microfluidizer® | 182 | 10,000 | 2 |

➔ HPH consumes as much as **7.5 times** power to achieve similar particle sizes.

### Uniformity of Distribution




### Repeatability




## Conclusion

- Microfluidizer® processors are well suitable for manufacturing nanoemulsion vaccine adjuvants.
- Microfluidizer® processor consumed **7.5 times less power** than the high pressure homogenizer.
- Microfluidized emulsions were **18-55% smaller** than the homogenized emulsions with the same energy input.
- Emulsions created by Microfluidizer® were **17-91% less polydisperse** than that created by high pressure homogenizer.
- The standard deviations of Microfluidized emulsions **(0.1-2.6)** were **much lower** than that of the homogenized emulsions **(3.8-14.8)**.


1. Vaccine adjuvants review, www.innivogen.com, 2011
2. Subunit vaccine delivery, Springer, 2015