



# Cambridge Biostability Ltd. Technology

Completely stable liquid vaccines  
and  
Disposable safety injectors



Bringing technology to life



## Summary

- 5 of 7 Key patents granted
- Stable liquid formulation proven
- Injector prototype produced
- Public/private partnership with PATH





# PATH/CBL Agreement

- Signed in Palace of Westminster London 25<sup>th</sup> Nov 2003
- Public/Private partnership
- PATH to assist development of CBL stable liquid vaccines
  - \$14 million from Gates Foundation
- CBL will license technology for public sector, developing world at low cost
- CBL retain rights in private sector



# Stability in Nature

- Anhydrobiotic organisms
- Can dry out completely (L)
- Stay dry for years
- Come back to life when wet (R)
- Contain inert sugar which forms glass on drying
- Stable at RT for over 120 years



*Selaginella lepidophylla*  
The “Resurrection Plant”





# Glass Stabilization



*30M year-old fossil  
insects in amber.*

**A “Model” of glass  
stabilised molecules**

## **SMOOTH, CONTINUOUS PROCESS:-**

- ***During drying;***
  1. **Molecules freely-mobile in sugar solution**
  2. **Becomes syrup as water evaporates**
  3. **Syrup solidifies as a glass**
  4. **Molecules immobilized in solid solution in glass**
  5. **No diffusion, no chemistry, no damage**
- ***On rehydration;***
  1. **Process reverses**

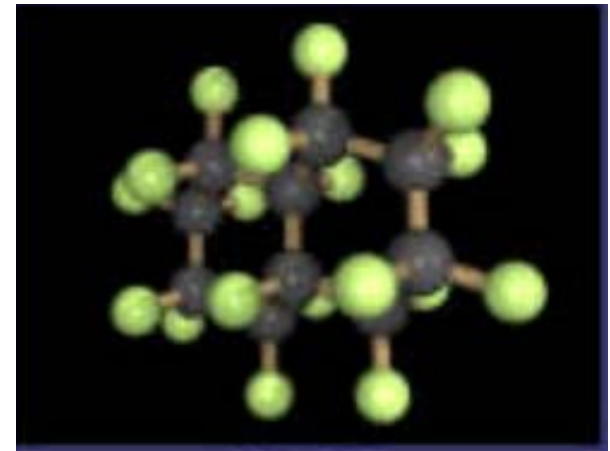




# Perfluorocarbons

*Completely stable injectable liquids*

- Fully fluorinated
- Strong F-C bonds
- Completely Stable
- No ozone depletion
- Miscible only with other PFCs





# Perfluorocarbons

## *COMPLETELY STABLE INJECTABLE LIQUIDS*

- Non-toxic
- Non-irritant
- High gas ( $O_2$  and  $CO_2$ ) solubility
- Low viscosity,
- Low surface tension,
- High density



“Liquid breathing”

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# PFC Clinical

- FDA and EMEA approved
  - Blood substitute (Oxygent™)
  - Neonatal respiratory distress (LiquiVent®)
  - Detached retina (Vitreon®)
  - Ultrasound Contrast agent (Optison®)
- Non-toxic, non-irritant,
- Volatile - Exhaled in breath
- High density; stable suspensions



“Liquid breathing”

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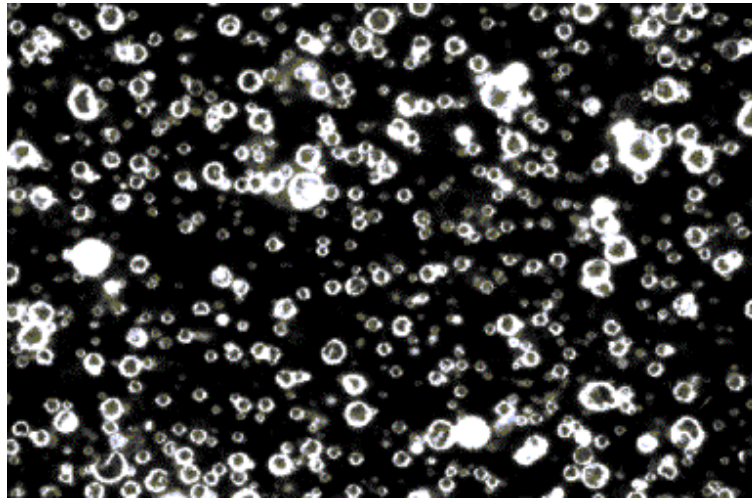






# Stable Liquids

## *Glass microspheres in Perfluorocarbon (PFC) Liquids*



- Spherical
  - Monodisperse
  - High Lubricity
  - Density-matched
  - Permanent Physical stability
  - Complete Chemical stability
- 
- Extreme Multivalency
  - Instantly injectable
  - Controlled Release
  - Non-hygroscopic
  - Water repellent

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# Physical Stability of Stable Liquids



**Left = Density-matched mixed glass in PFC**

**Middle = Sugar glass in oil**

**Right = Sugar glass in PFC**





# Advantages

- Ready-to-inject
  - Physically stable
  - Chemically stable
  - No preparation in the field
- Pre-filled
- Minimal skills
- Bacteriostatic
  - No thiomerosal
- High multivalency
- Controlled release
  - Single shot vaccination ?





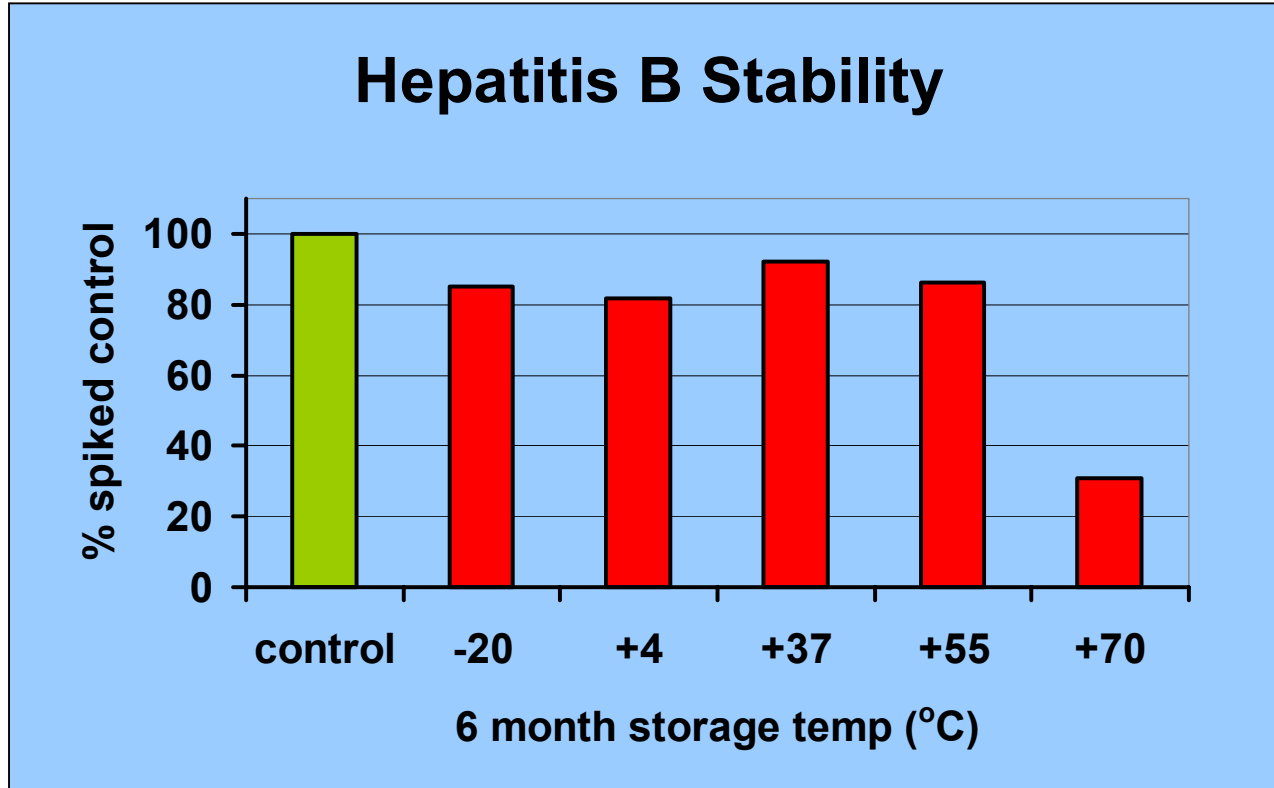
# Commercial Vaccine Projects

- **Products**
  - Conjugate Meningitis A vaccine
    - Successful *in vitro* and pre-clinical trials
  - Hepatitis B recombinant
    - Successful *in vitro* and pre-clinical trials
  - Hib conjugate
    - Ongoing *in vitro* and pre-clinical trials
  - Tetanus toxoid vaccine
    - Successful *in vitro* and pre-clinical trial
    - In collaboration with NIBSC
- **Development underway**
  - Measles
- **Development under discussion**
  - Pentavalent vaccine (DTaP, Hib, hepB,)
  - BCG

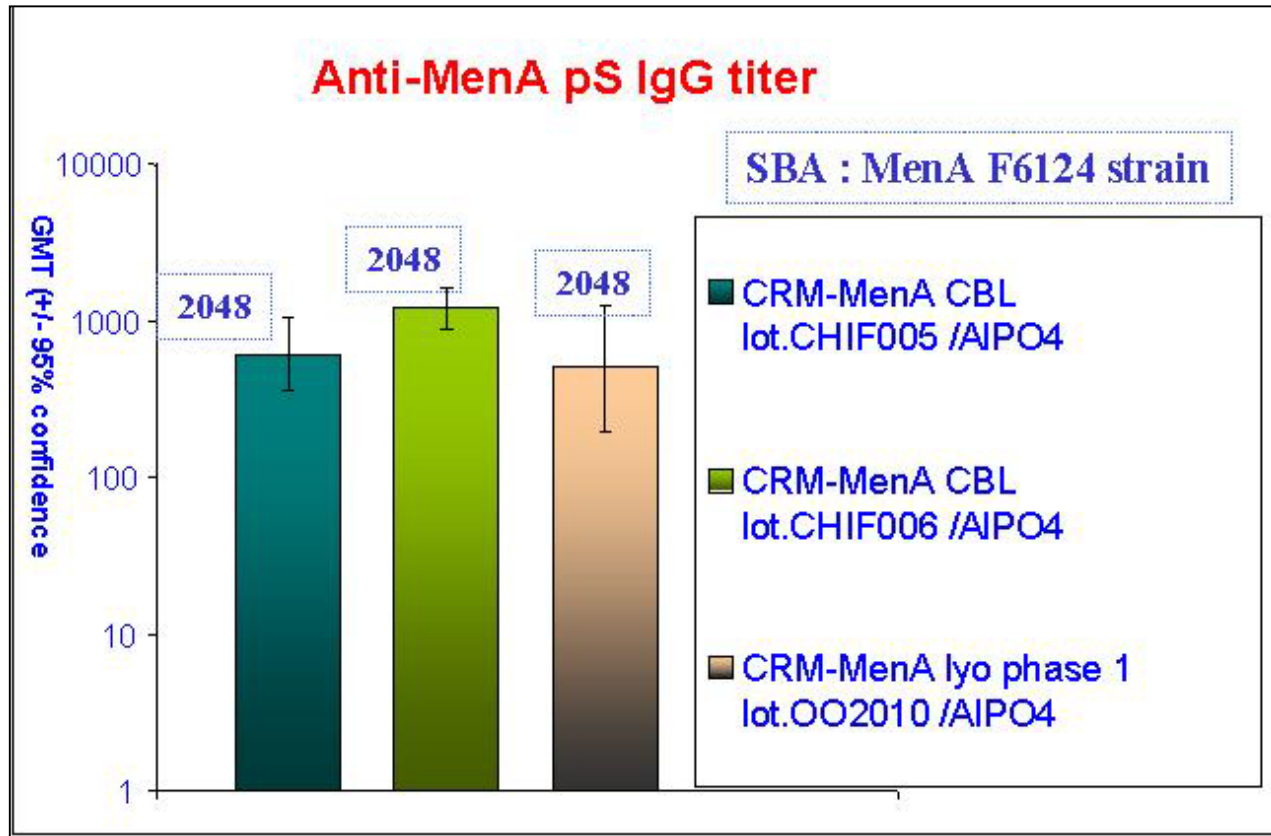




# Storage Stability Hep B



# Meningitis A conjugate

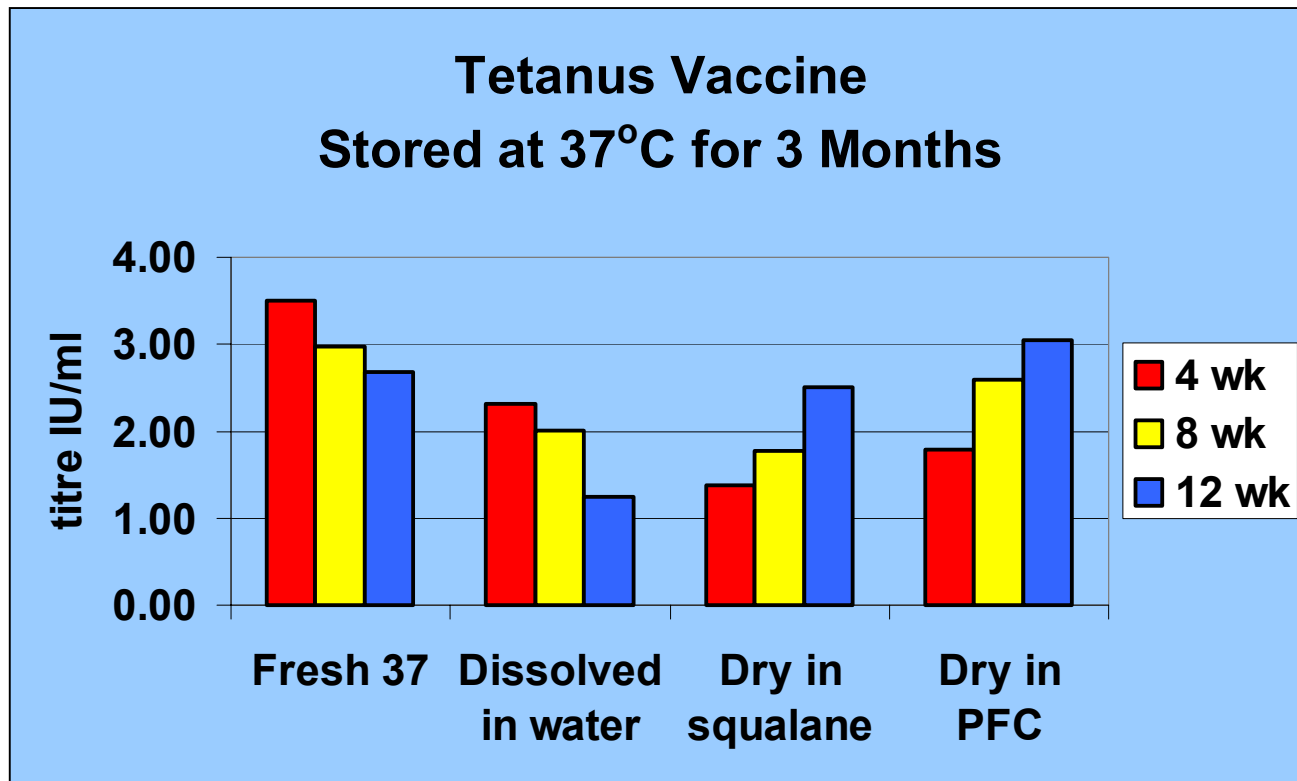


- Groups of 10 mice immunised on day 0 and 28 and bled on d 42



# Stability of PFC based vaccine

Controlled Release ?



Data from UK National Institute of Biological Standards and Control



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# Disposable Injectors 1- Syringe Vaccinator



**Ready**



**Used & Locked**

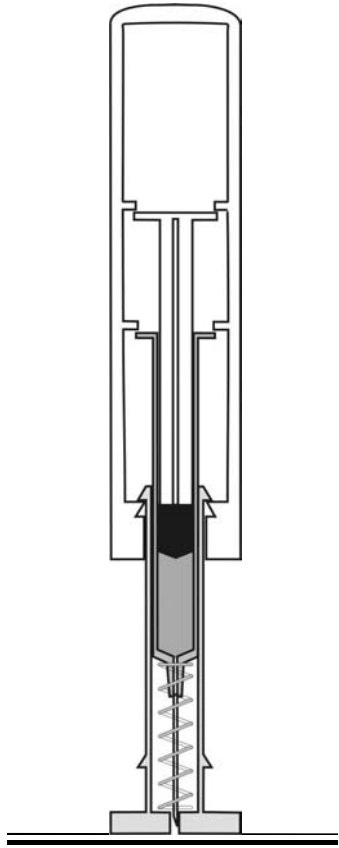
- Injection-moulded case encloses a pre-filled syringe
- Hand pressure suddenly snaps rings
- A single downward movement of cap;
  - Inserts the needle to pre-set depth
  - Then delivers the pre-filled dose
  - Then retracts needle and locks the device for disposal





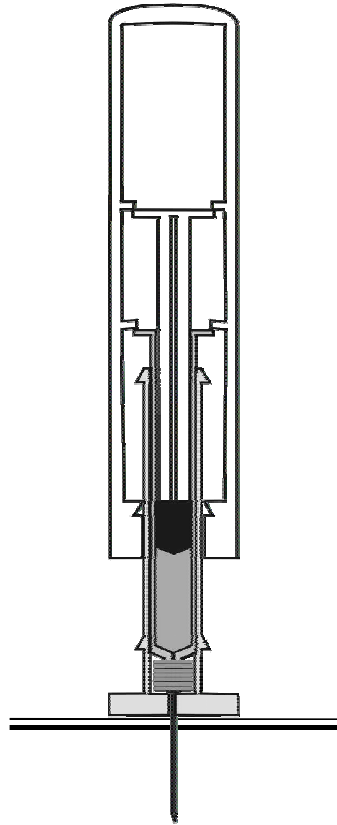


# Vaccinator Injection Sequence

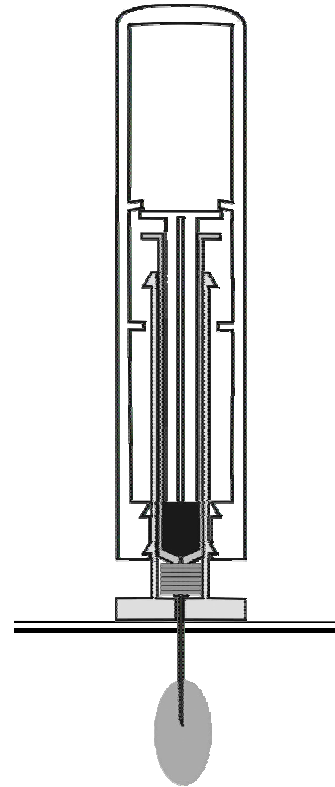


Remove adhesive transfer foil & apply to skin.

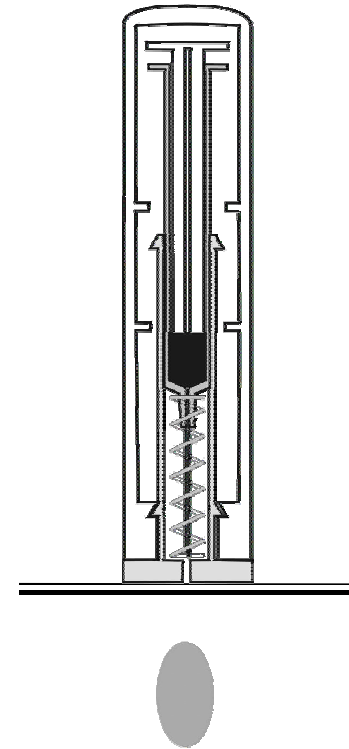
Hand pressure snaps first ring.



Second snapping pushes barrel to insert needle then snaps over flange.



Third snapping depresses plunger to inject dose then snaps.



Spring retracts syringe .  
Disabled device locks safe.

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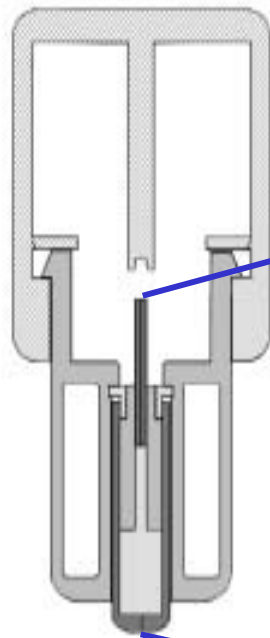




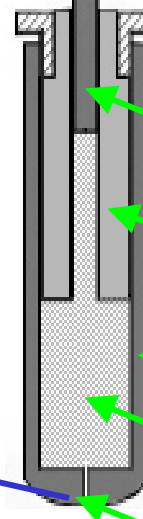
# Disposable Injectors 2: Snapjet®

## SNAPJET® LIQUID JET INJECTOR

The Nozzle is pressed against patient's skin by modest hand pressure on cap



### Dosage vial

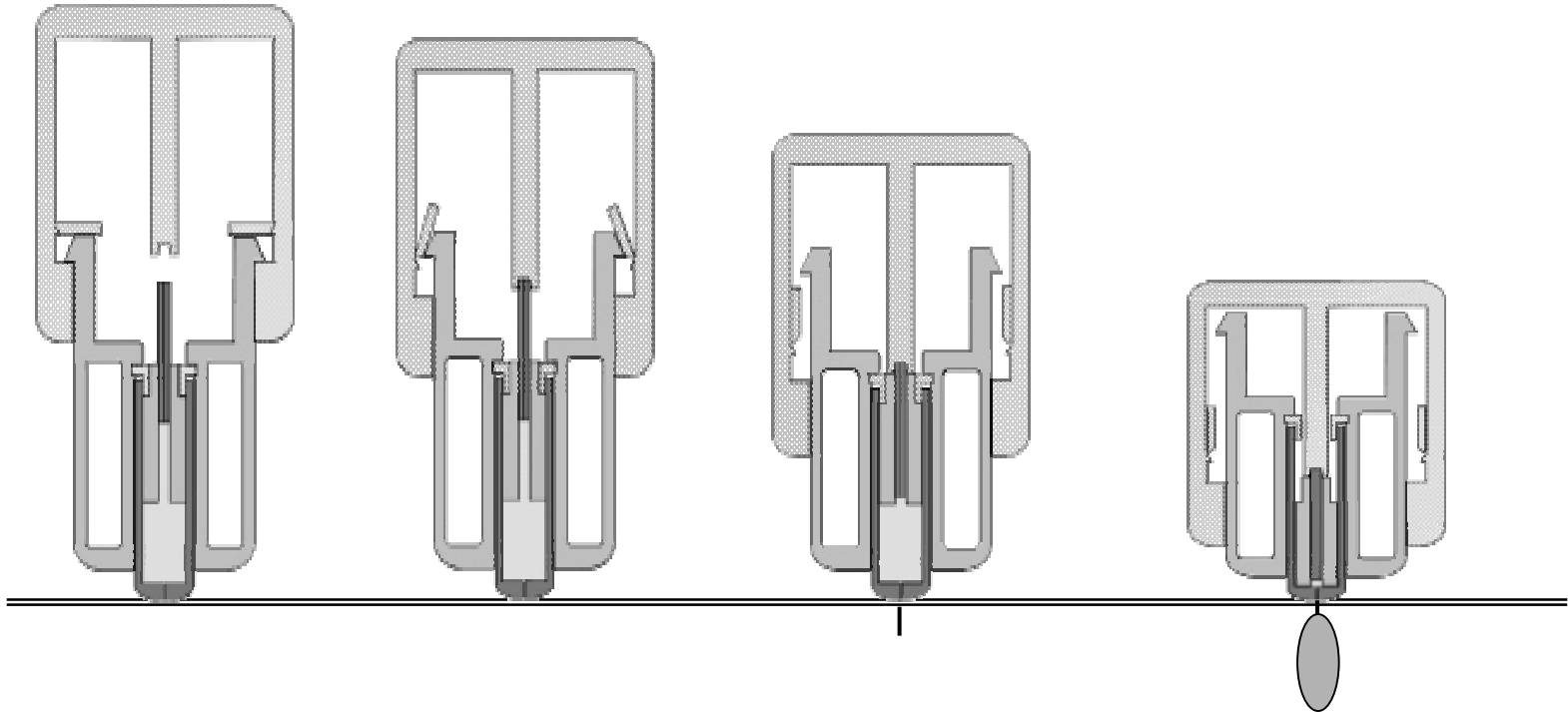


- Retaining ring
- Narrow central plunger
- Wide annular plunger
- Outer capsule with
- Vaccine
- jet nozzle





# Snapjet<sup>®</sup> Injection Sequence



**Hand pressure  
seals nozzle  
against skin**

**Tabs break.  
Finger strikes  
narrow plunger**

**Narrow plunger drives  
high-pressure jet  
through skin**

**Finger drives wide  
annular plunger to  
deliver dose down track**



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# CBL Vaccine Technology

- **Completely stable liquid Vaccines**
  - High Multivalency
  - Controlled release
- in
- **Disposable safety Injectors**
  - Safe
  - Simple
  - Cheap

