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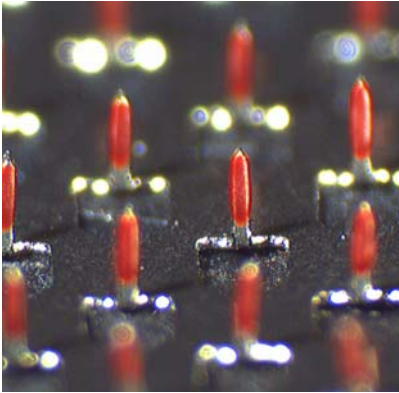
PCPP Coated Microneedles -

Integrating Immunoadjuvants and Intradermal Delivery

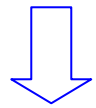
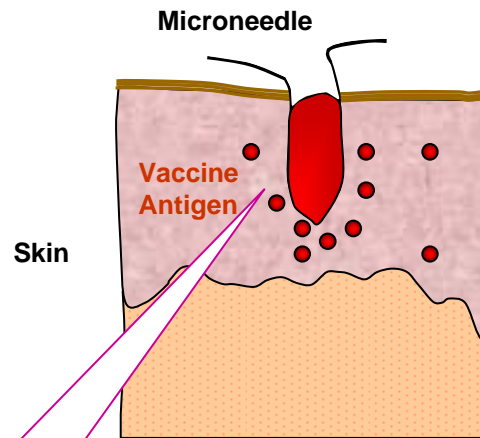
**Alexander K. Andrianov**



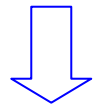
# Coated Microneedles for Vaccine Delivery



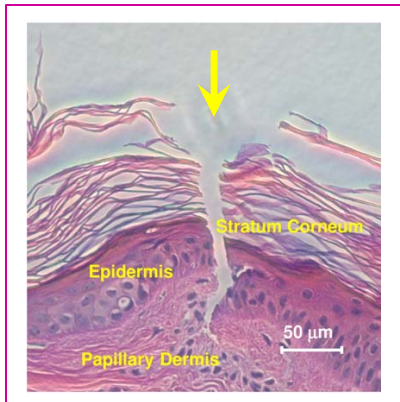
Microneedles Containing Vaccine Antigens Target Skin Dendritic Cells



Enhanced/Modulated Immune Responses



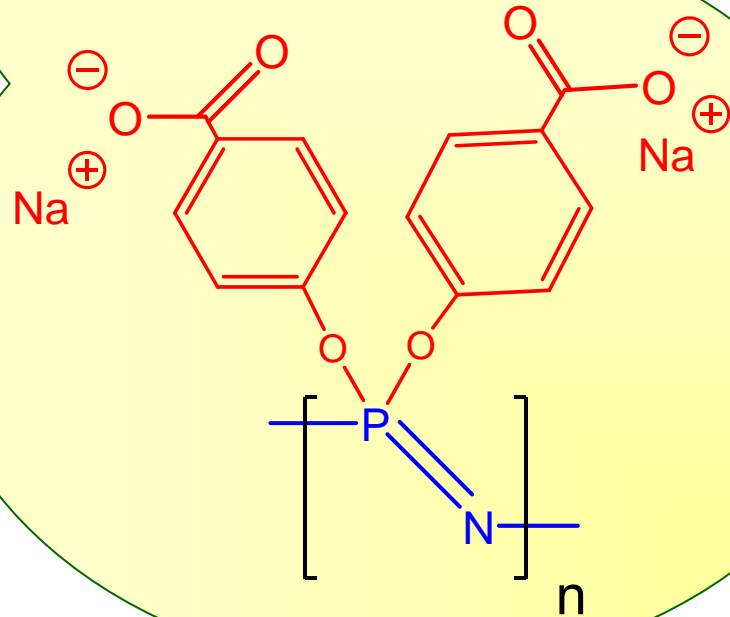
Histological Section



Compatibility with Adjuvanted Vaccines? ?

# PCPP: Poly[di(carboxylatophenoxy)phosphazene]

- Water-Soluble Synthetic Polymer
- Well-Defined Structure
- High Molecular Weight



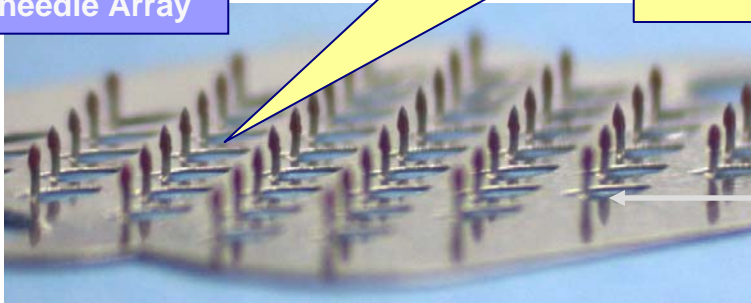
- Biodegradable
- Benign Degradation Products

- Potent IM Adjuvant
- Proven In Vivo Performance
- 23 Antigens in 11 Animal Models

# Coated Microneedles Polyphosphazene Microneedle Approach

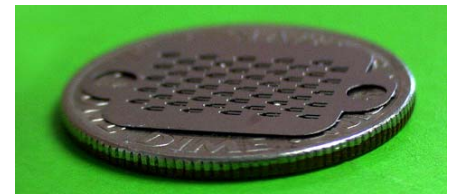
Micro Dip-Coating Process Employed

Microneedle Array



SOLID FORMULATION:  
PCPP – VACCINE

Metal  
Support



# PCPP Adjuvanted Microneedles – Key Questions

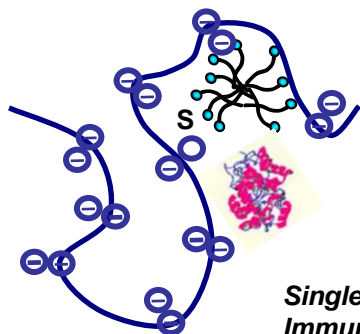
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- **Stability Of PCPP-Vaccine Formulations in The Microfabrication Process**
- **Material Properties of PCPP as a Microfabrication Agent**
- **Performance as ID Adjuvant**

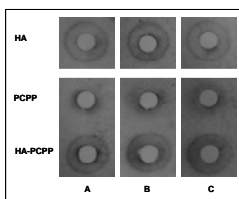
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**STABILITY OF PCPP-VACCINE FORMULATIONS  
IN THE MICROFABRICATION PROCESS**

# PCPP Stabilized H5N1 Influenza Vaccine Formulations

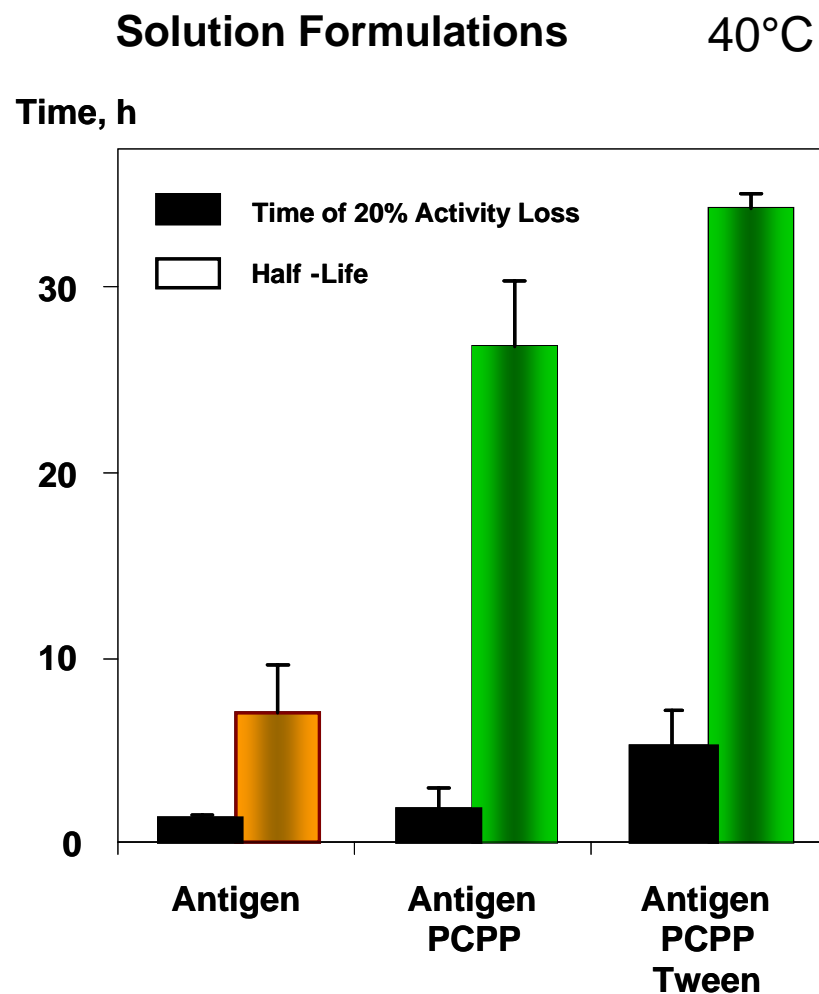


Single Radial Immunodiffusion (SRID) Data



## Microneedle Fabrication

Coating Cycles	Loading, $\mu\text{g}/\text{array}$		Efficiency of H5N1 Antigen Incorporation, %
	PCPP	Antigen	
38	16	0.4	100
50	35	0.8	100



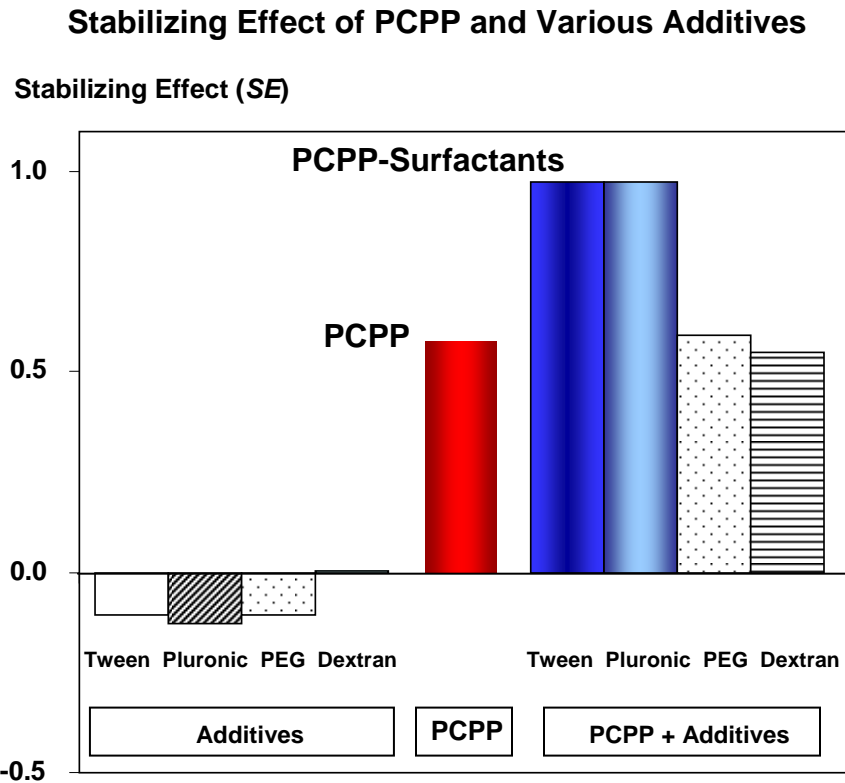
# PCPP Stabilizes Protein Formulations

## Horseradish Peroxidase (HRP)

Half-Life, min

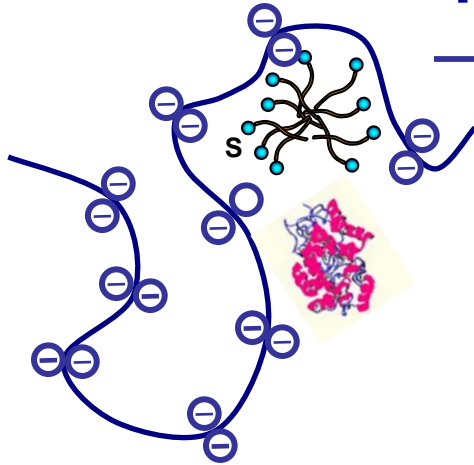
HRP	9
HRP-PCPP	34
HRP-PCPP-Tween®	85

Thermoinactivation in Solution (70°C)

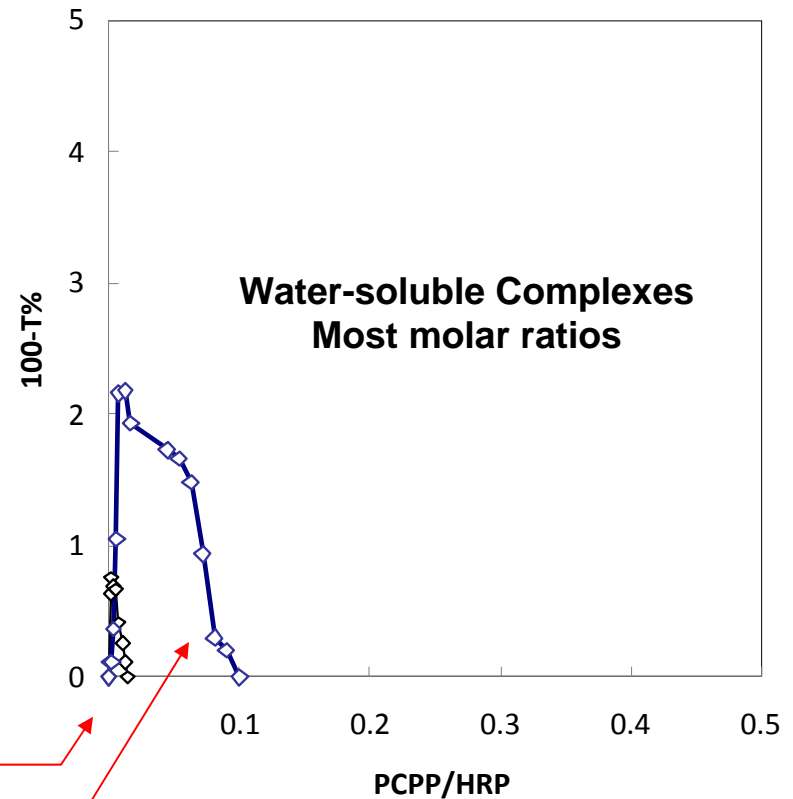




# PCPP-Protein Complex Formation



*Turbidimetric titration*



Water-Insoluble Complexes in Excess of Protein

No Tween: **HRP:PCPP = 440:1**

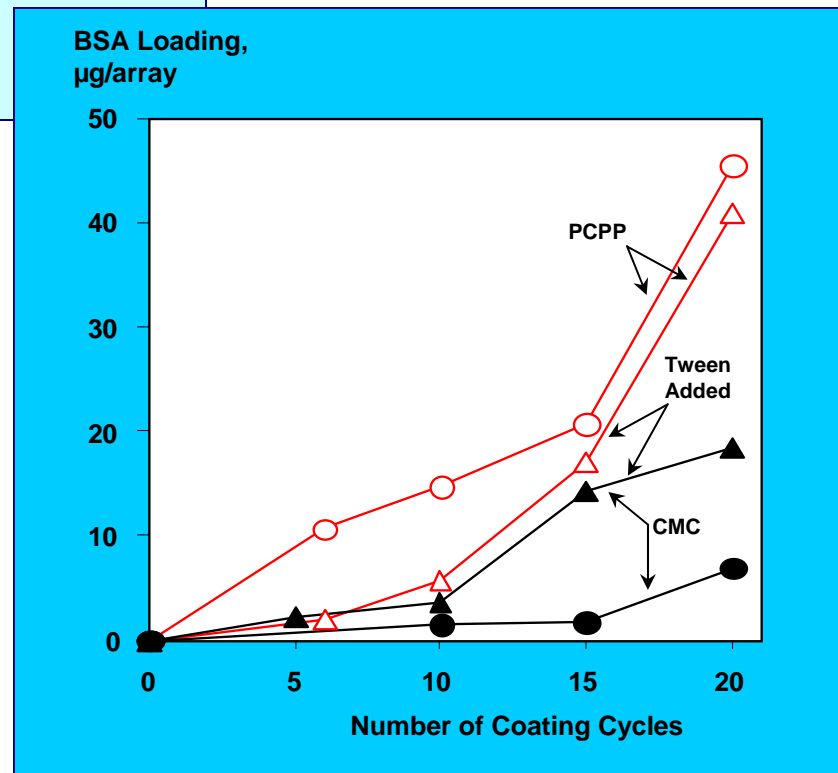
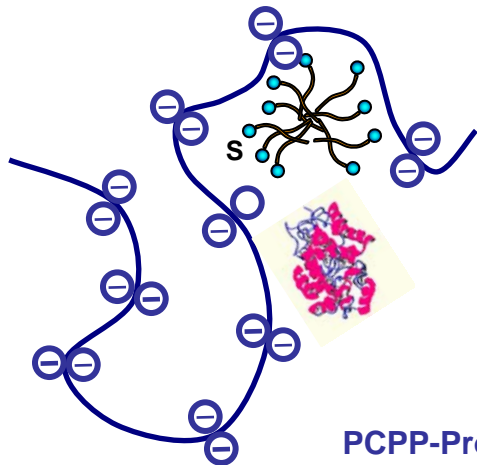
Tween: **HRP:PCPP = 103:1**

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## **Material Properties of PCPP as a Microfabrication Agent**

# PCPP is Effective as A Coating Agent

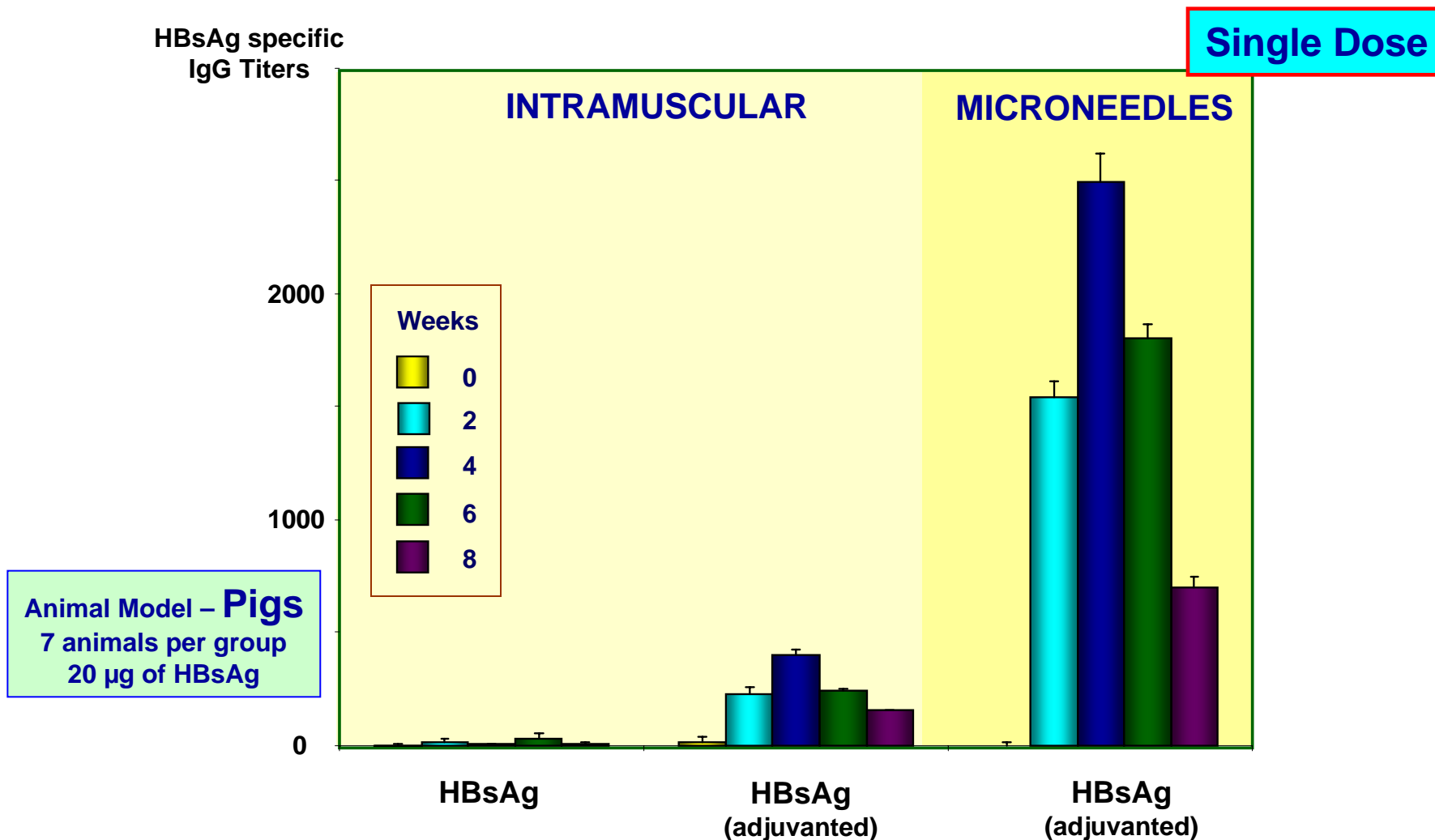
- Performance of PCPP Is Comparable to One of Carboxymethylcellulose (CMC)
- Dependence on Surfactant is Reduced



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## PERFORMANCE AS **ID** ADJUVANT

# PCPP Microneedles – SUPERIOR LEVEL of Immune Response

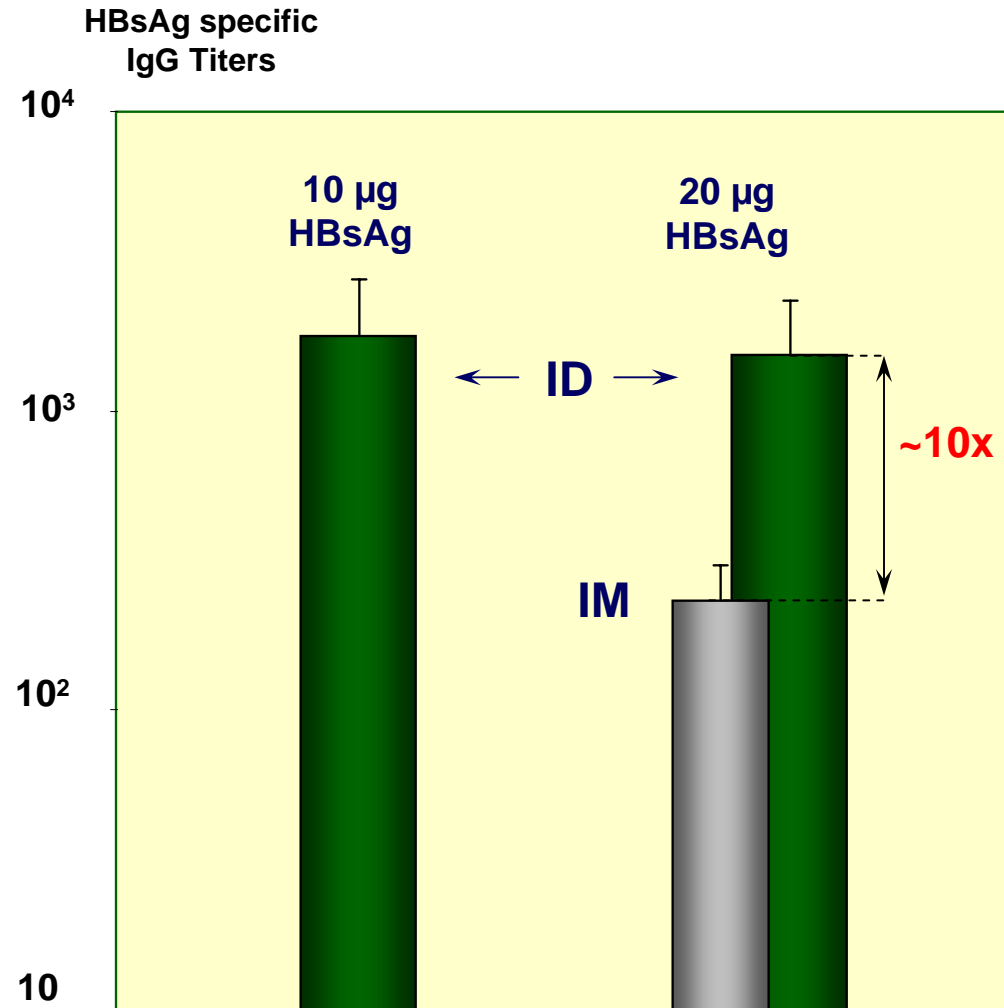


# Antigen Sparing Effect for PCPP Microneedles

## Intradermal Immunization (ID) Using Microneedles

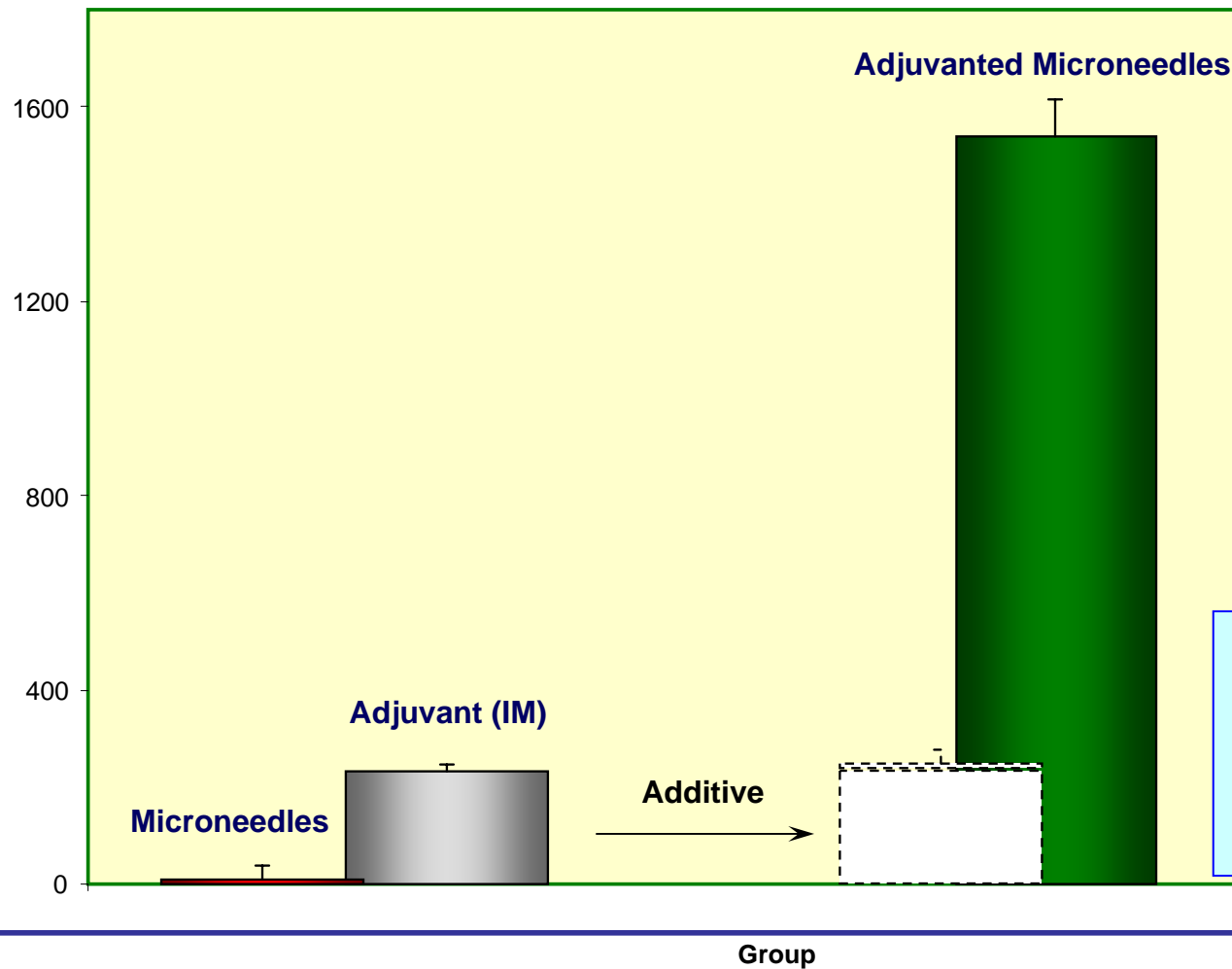
- 10  $\mu$ g ID > 20  $\mu$ g IM (~10x)
- 10  $\mu$ g ID = 20  $\mu$ g ID

Animal Model - Pigs  
7 animals per group  
Week 2 data  
HBsAg  
Adjuvanted formulation  
Single Immunization



# Synergistic Effect of Microneedle Delivery and Immunoadjuvant

HBsAg specific  
IgG Titers



Animal Model - Pigs  
7 animals per group  
Week 2 data  
HBsAg  
Adjuvanted formulation  
Single Immunization

# Key Advantages of PCPP For Microneedle Vaccine Delivery

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- Potent Immunoadjuvant Properties

  - Synergistic effect

  - Dose Sparing

- Protein/Antigen Stabilizing Capability

  - Enables encapsulation of sensitive vaccines

- Excellent Microfabrication Properties

  - Decreases reliance on surfactants



## ACKNOWLEDGEMENTS

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