

**NEXT-GENERATION BIOSPECIMEN PRESERVATION  
AT AMBIENT TEMPERATURE  
BASED ON THE USE OF MICRON-SCALE  
SCAFFOLDS**



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# IntegenX Products for Ambient Temp BioSample Preservation

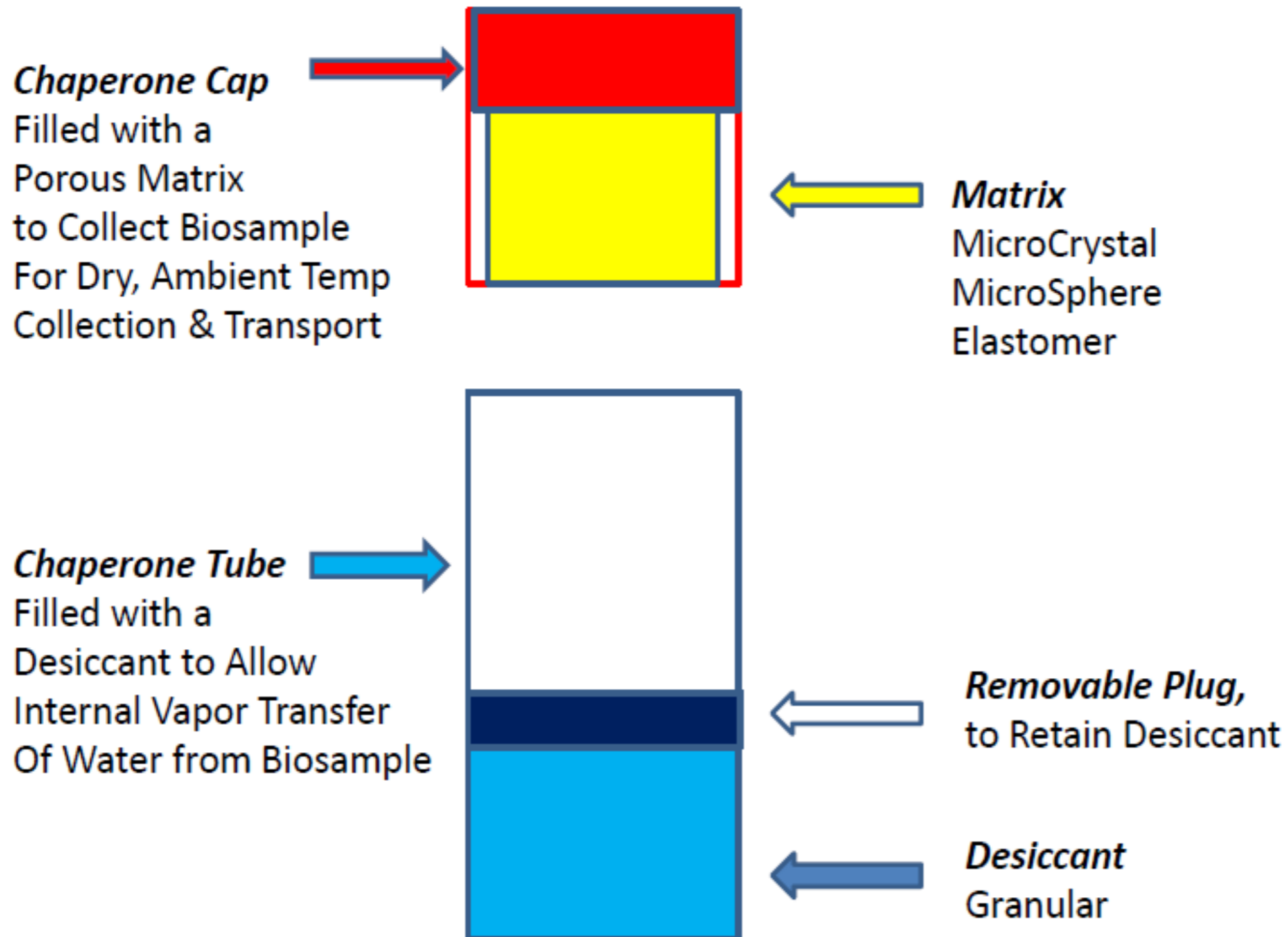
- **IntegenX has Developed Multiple Products for Dry, Ambient-Temp Biosample Preservation**
  - GenTegra-DNA      Purified DNA
  - GenTegra-RNA      Purified RNA
  - GenPlates          Raw Blood, for DNA Purification (GE-FTA)
  
- **All Current IntegenX Products are Based on Similar Principles**
  - Preservation by Air-Drying
  - Addition of Chemical Stabilizers (Nuclease and Oxidation)
  - Solid Physical Matrix as a Sample Support

# The DARPA “Matrix-Chaperone” Project

- **Recent DARPA & DHS Funding has Allowed Development A New BioSpecimen Technology: “Matrix Chaperone”**
  - Raw Samples Collected in the Field or in a Clinic
  - DNA, RNA, Small Molecule & Protein Analytes
  - Materials Science → **“Matrix”**
  - Self-Contained Collection, Shipping & Storage Device → **“Chaperone”**
- **The Matrix-Chaperone Concept**
  - Apply a Raw BioSample to a Wafer of Porous Matrix
  - ***Instantaneous Wicking*** of the BioSample into the Wafer
  - ***Instantaneous Saturation*** of the Wicked BioSample with Stabilizers
  - ***Immediate Enclosure*** within the Chaperone Tube
  - ***In Situ Physical Desiccation***
  - ***Multiple Form-Factors***: Compatible with the Bench or Autonomous Devices

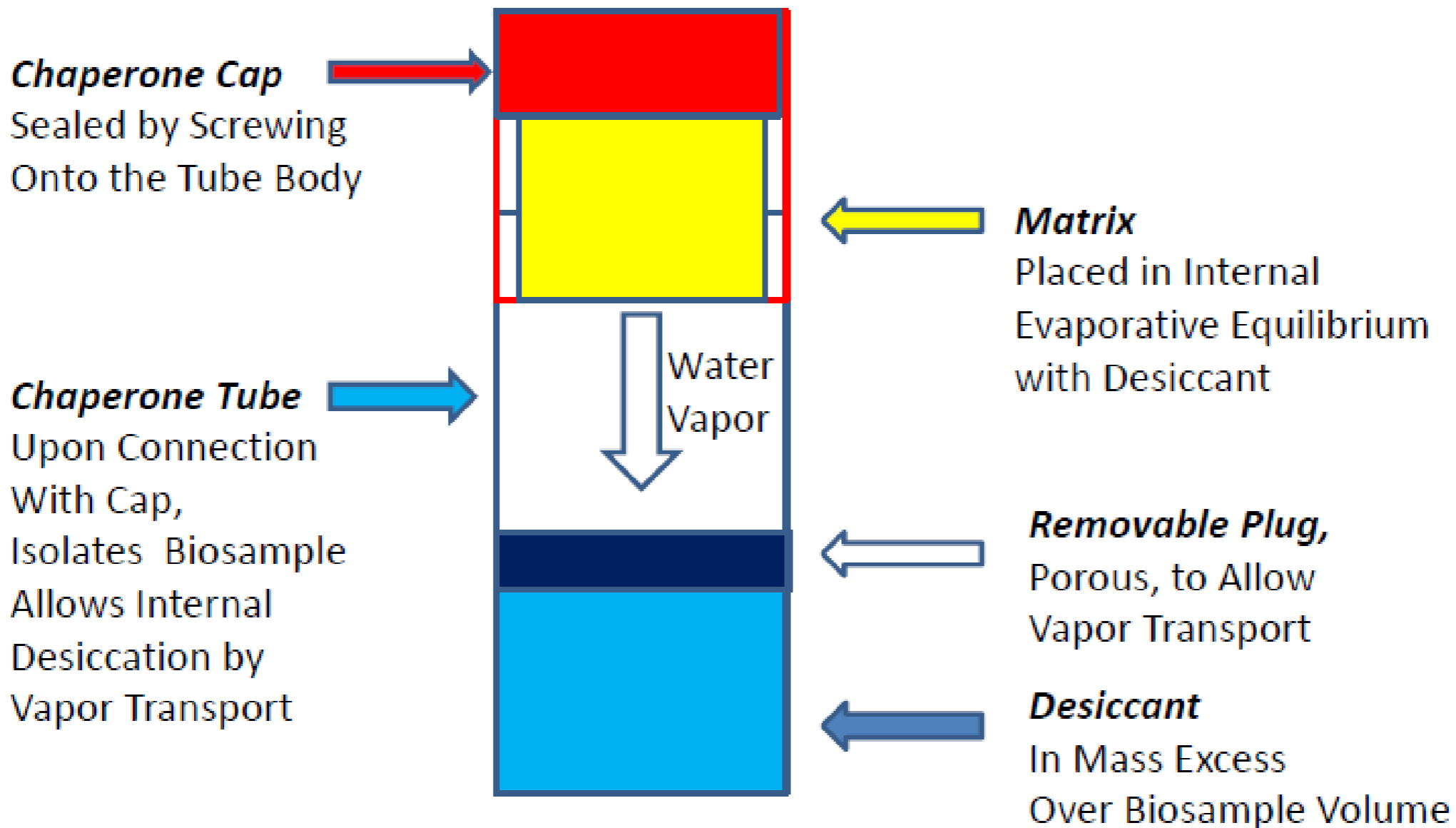
# Matrix-Chaperone: Matrix in The Cap Desiccant in the Body of Cylindrical Chaperone

## Matrix-Chaperone Concept



# Matrix-Chaperone (Sealed)

## Matrix-Chaperone Concept



# Matrix-Chaperone is Flexible: Multiple Routes to Sample Recovery

- **Three Classes of Porous Matrix: Rehydration and Recovery**


- MicroCrystal            Dissolve
- MicroSphere            Fluidize Spheres
- Elastomer                Squeeze

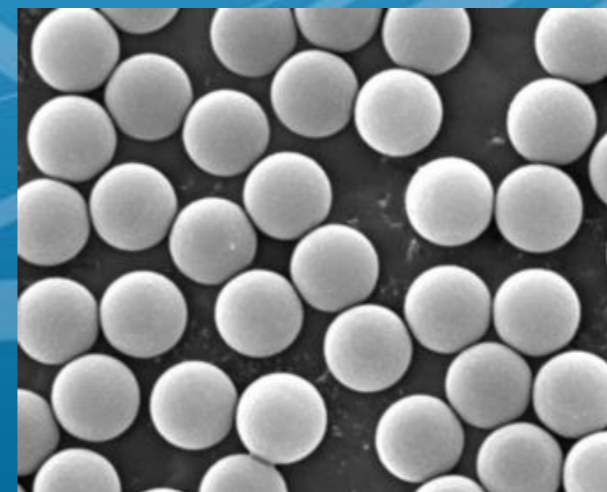
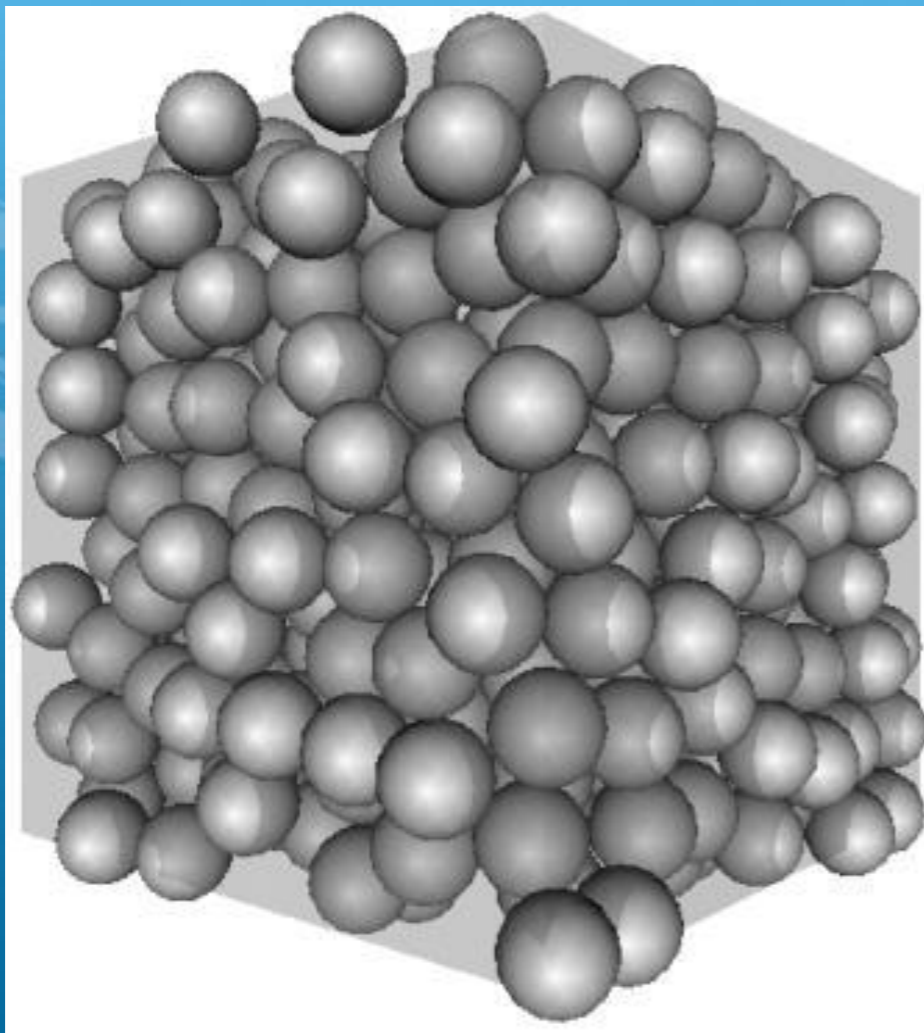
- **All Three Matrices have Common Properties**

- Pore size: 500uM
- Open Pores
- Form into Wafers
- Inexpensive and Scalable to Mass Production

# MicroCrystal & MicroSphere Molded into Porous Wafers with a Bonding Agent

**Randomly-Packed  
Spheres or Cuboids  
Pore Size @  $\frac{1}{2}$  Diameter  
Pore Volume @  $1/\pi$  Volume**

1,000um  




**MicroCrystals**  
Water-Soluble  
Bond into Wafers  
With Water & Stabilizer

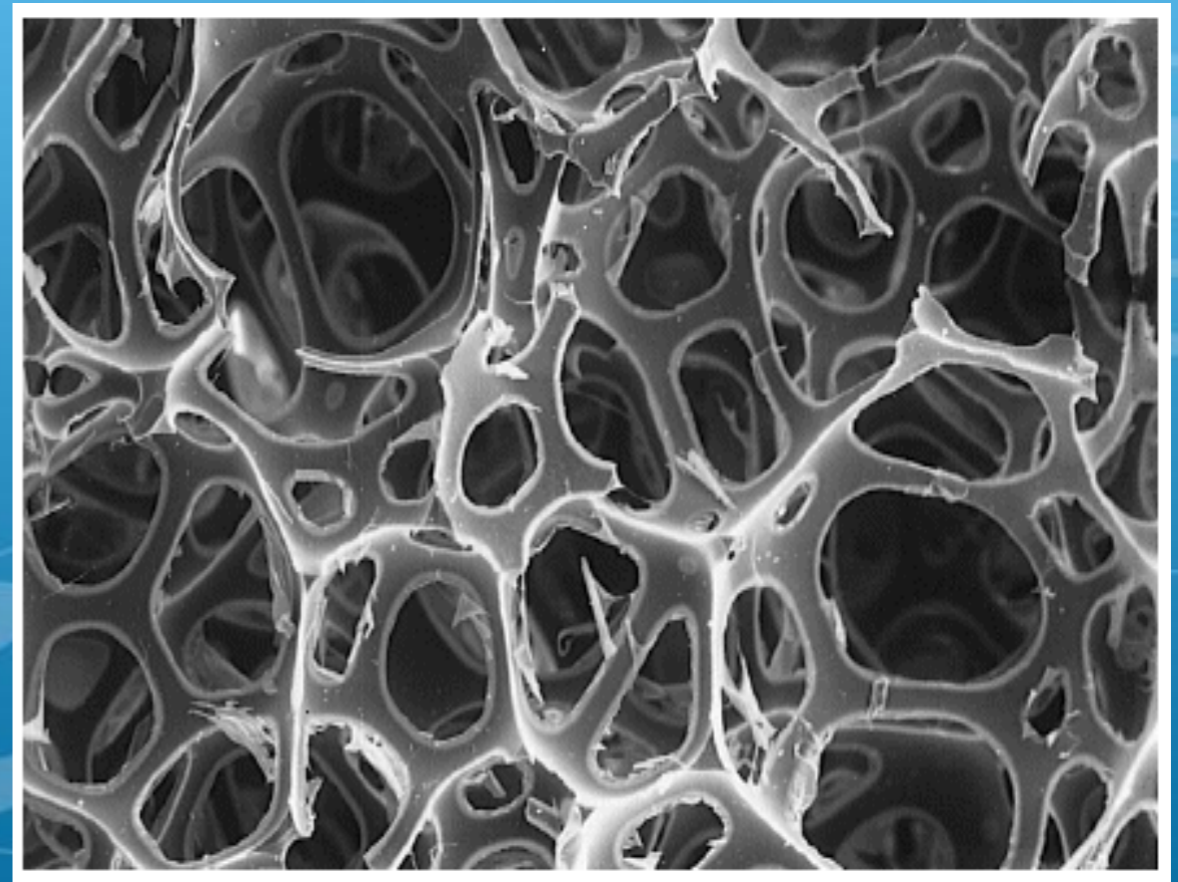
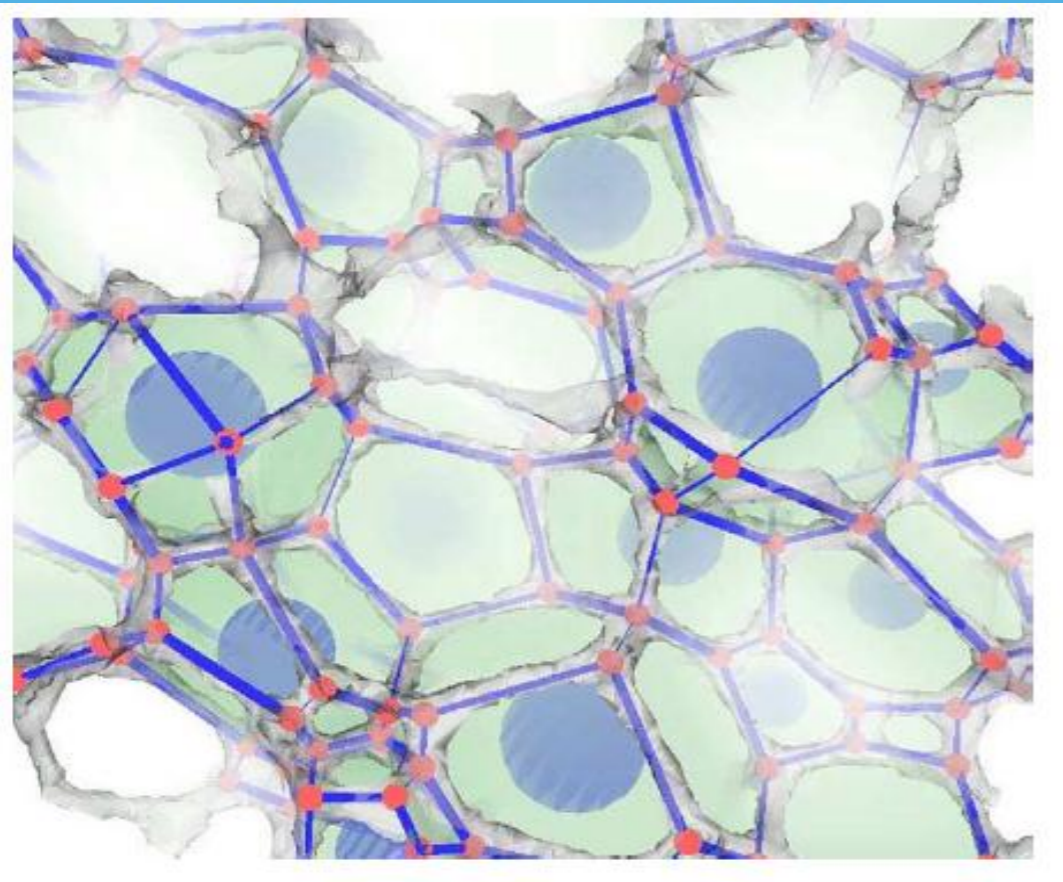
**MicroSpheres**  
Plastic  
Bond into Wafers  
With Water & Stabilizer  
& Bonding Agent

# Elastomer Wafers Fabricated by Dye Cutting

Elastomeric Foams have Tube-Like Pores  
3D Honeycomb “Bubbles” Fuse to Forming 3D Polygons

Pore Model From Tomography

Elastomer Data, SEM



1,000um





# Flexibility Resulting from the Three Different Matrices

- **Elastomer**

- **Swabs, Collect up to 1mL**
- Sample Collection from Surfaces and Cavities (Nares, Throat, Cheek)
- Recovery by Mechanical Compression

- **MicroCrystal**

- **Fluid, Collect up to 1mL**
- Sample Collection from Finger-Prick, Heel-Prick, Eye-Dropper, Pipettes
- Recovery by MicroCrystal Solvation

- **MicroSphere**

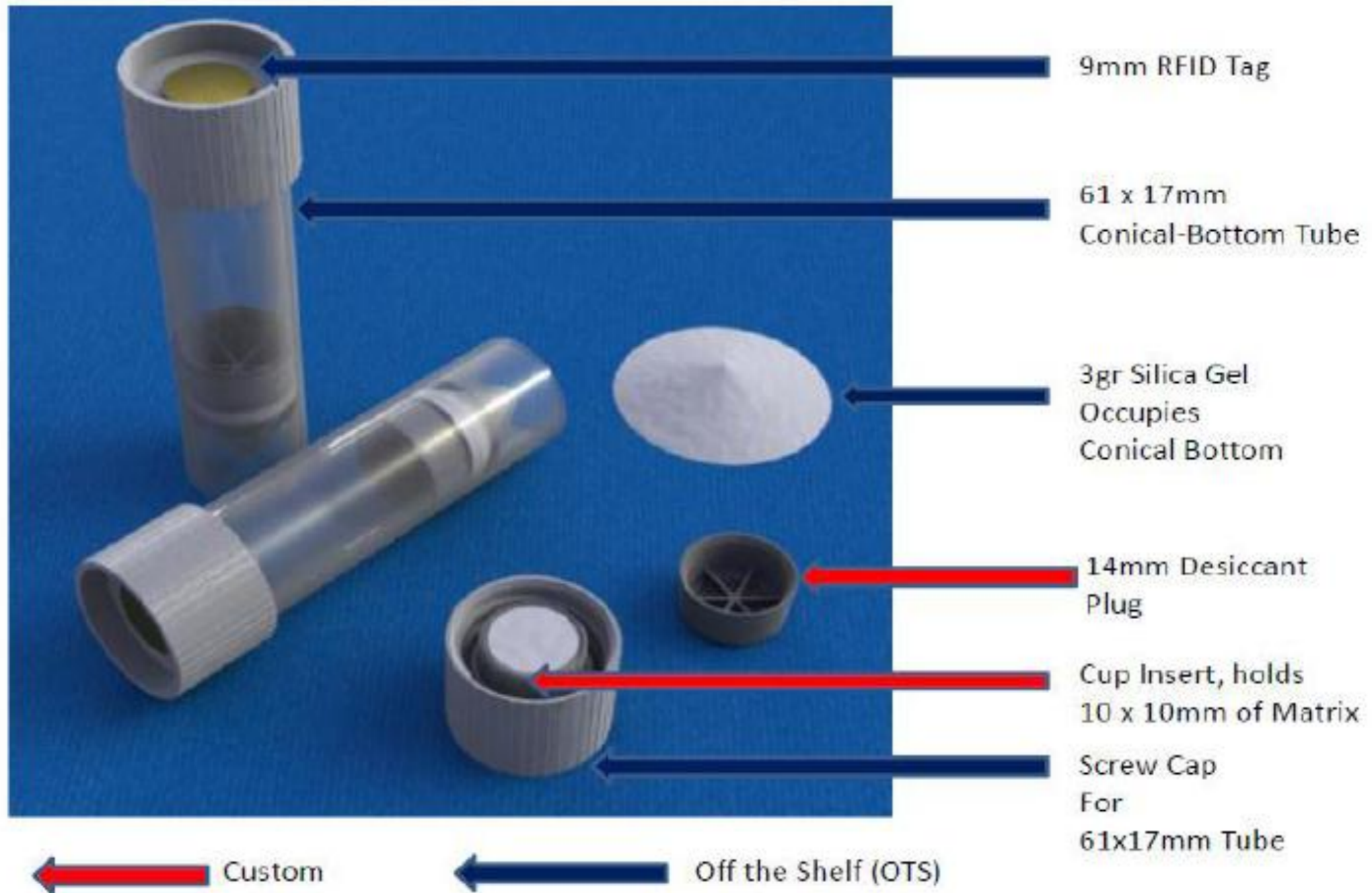
- **Fluid, Collect up to 1mL**
- Sample Collection from Finger-Prick, Heel-Prick, Eye-Dropper, Pipettes
- Recovery by MicroSphere Suspension

# Flexibility Resulting from Chaperone Design

- **Size and Shape Can be Altered as Needed**
  - Range of Wafer Volume from **50uL to 1,000uL**
- **Matrix-Chaperone Assembly is Simple & Inexpensive**
  - MicroCrystal & MicroSphere: Added like Gun-Powder in a Shell
  - Elastomer: Added like a Cork
  - Desiccant: Added like Gun-Powder in a Shell
- **Matrix Chaperone Compatibility with Labelling Technologies**
  - 2D Bar-Code, RFID, GPS
- **Matrix-Chaperone Compatibility with Downstream Analysis**
  - Manual Recovery at Lab Bench
  - Automated Recovery at Lab Bench
  - Direct Coupling to Autonomous Devices: Jump-Drive Model

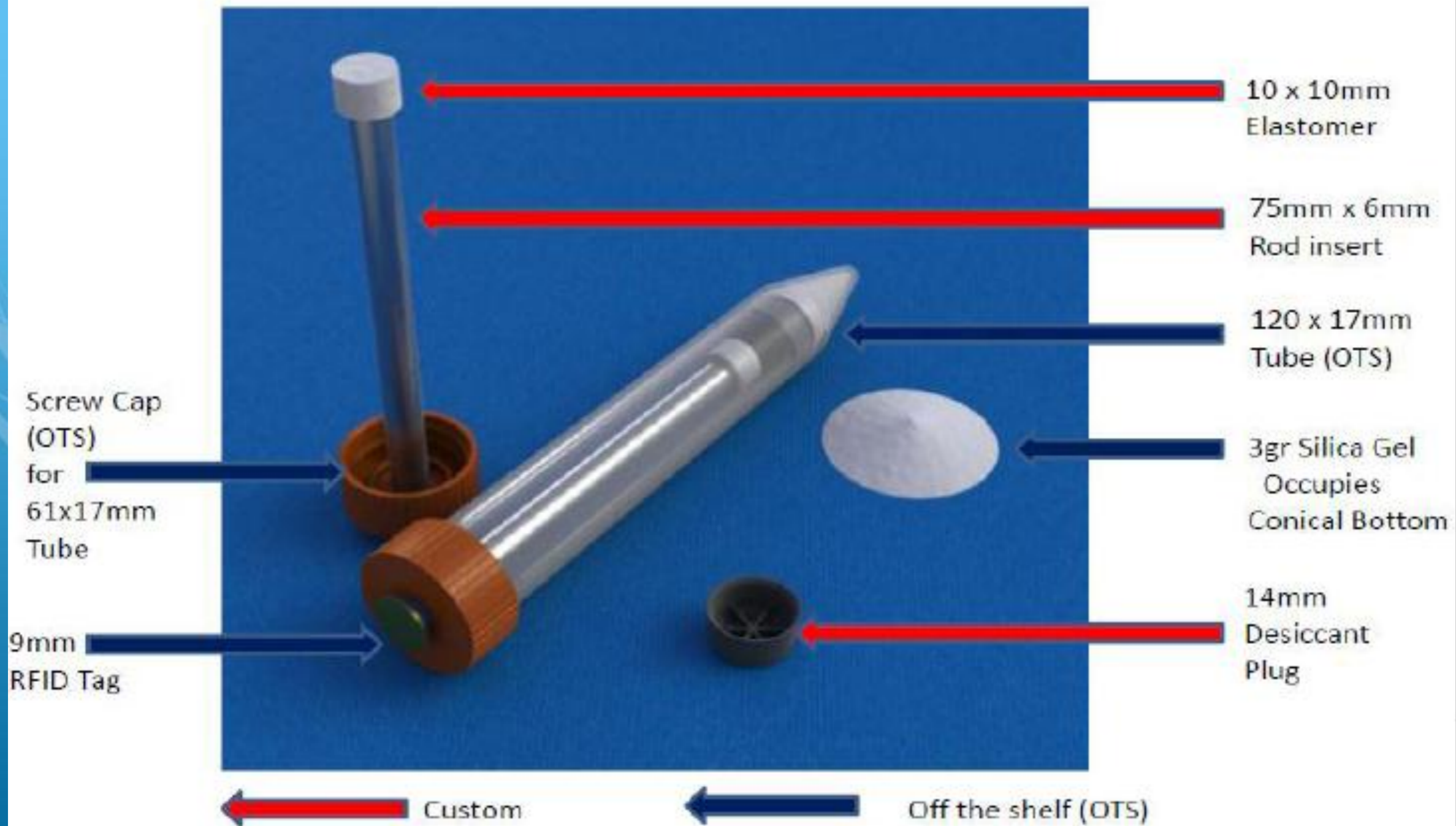
# Plastic Chaperone, 600uL Matrix MicroSphere or MicroCrystal

Hybrid [**Custom**+ Off-the-Shelf] Matrix-Chaperone

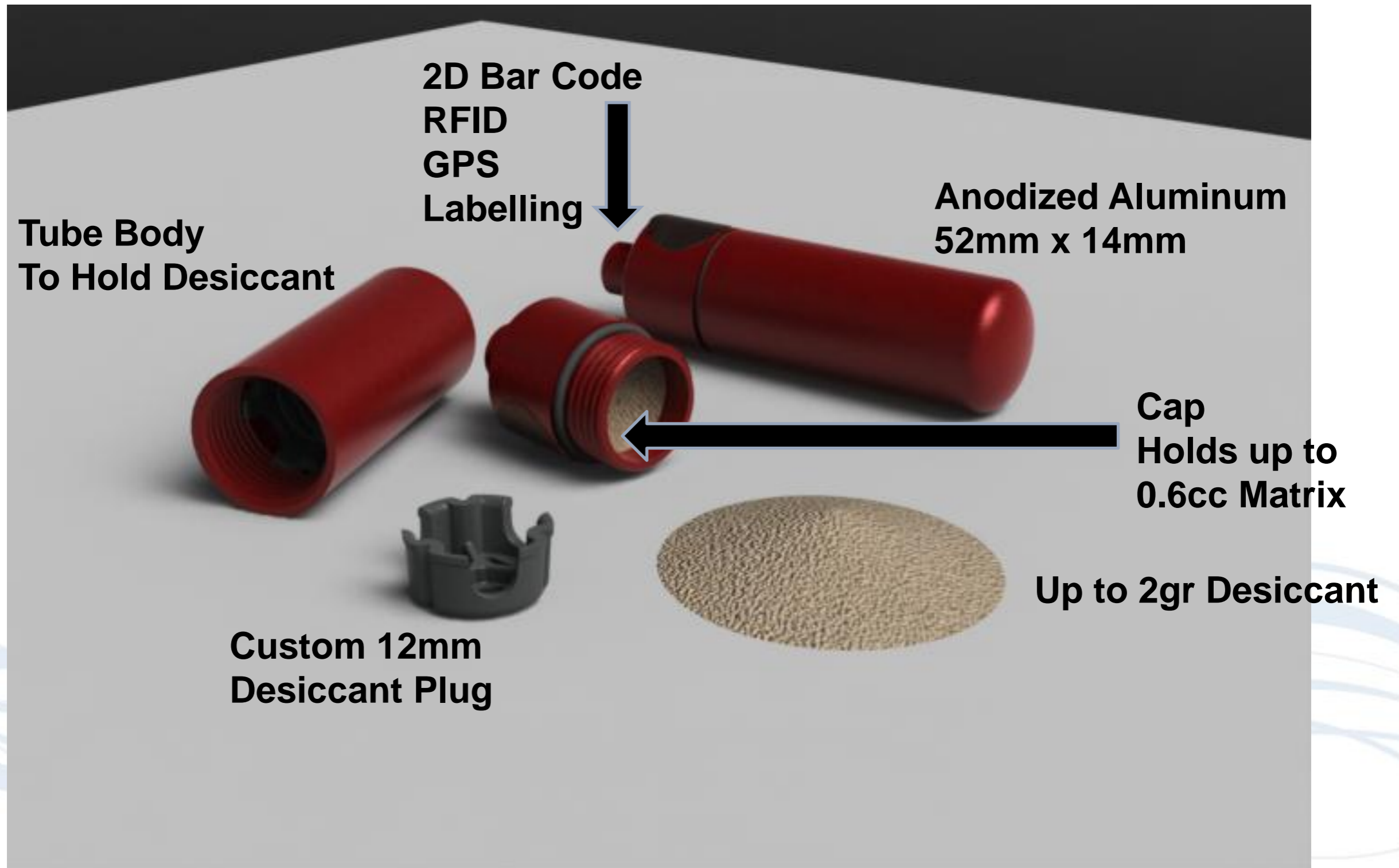


# Plastic Chaperone, 600uL Matrix 6cm Elastomer-Swab

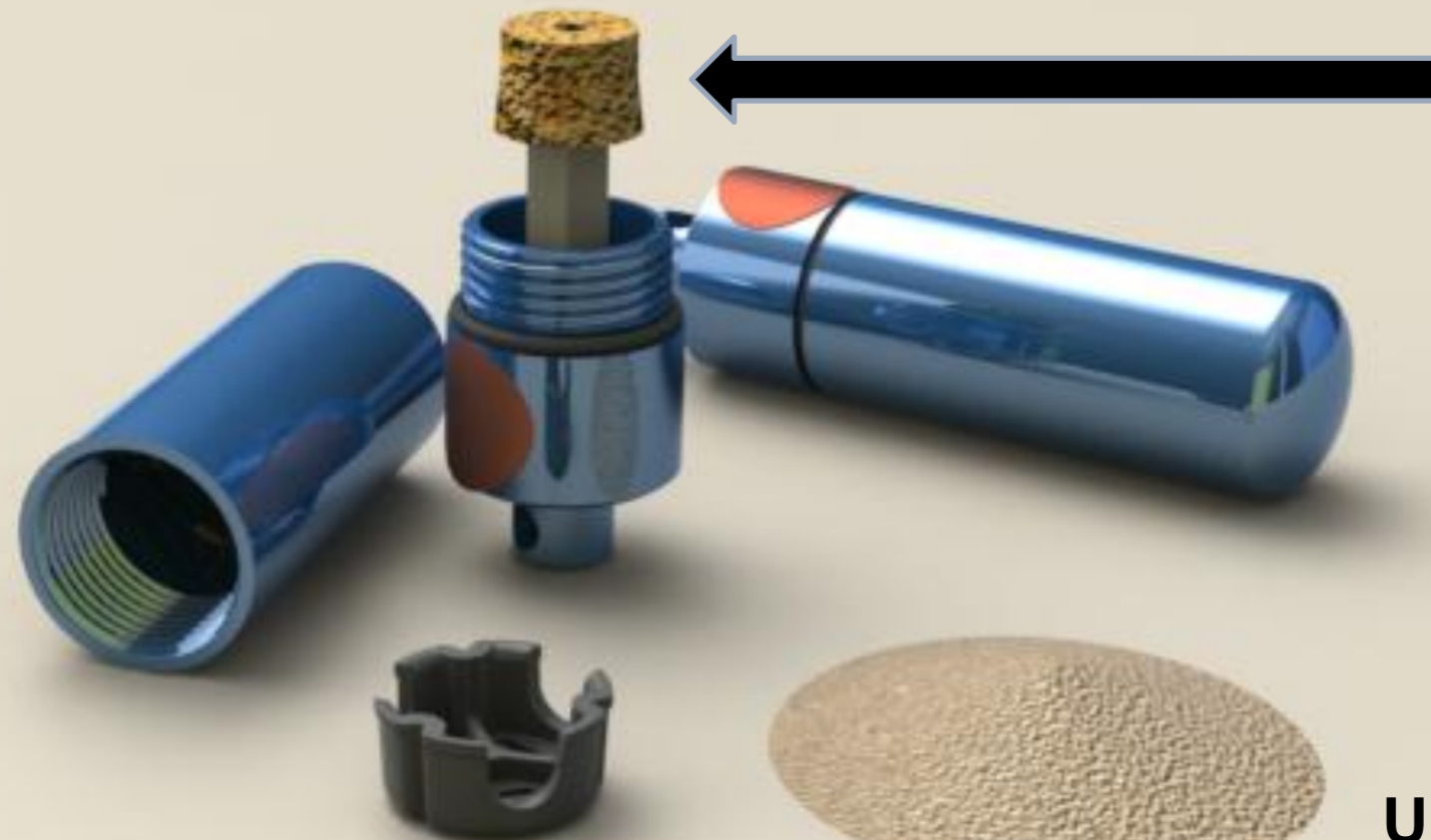
## Hybrid [**Custom**+ Off-the-Shelf] Chaperone Assembly



# Aluminum Chaperone, 600uL Matrix: MicroCrystal & MicroSphere



# Anodized Aluminum Chaperone, 600uL Elastomer “Mini Swab”



**Elastomer  
Holds up to  
0.6cc Matrix**

**Custom 12mm  
Desiccant Plug**

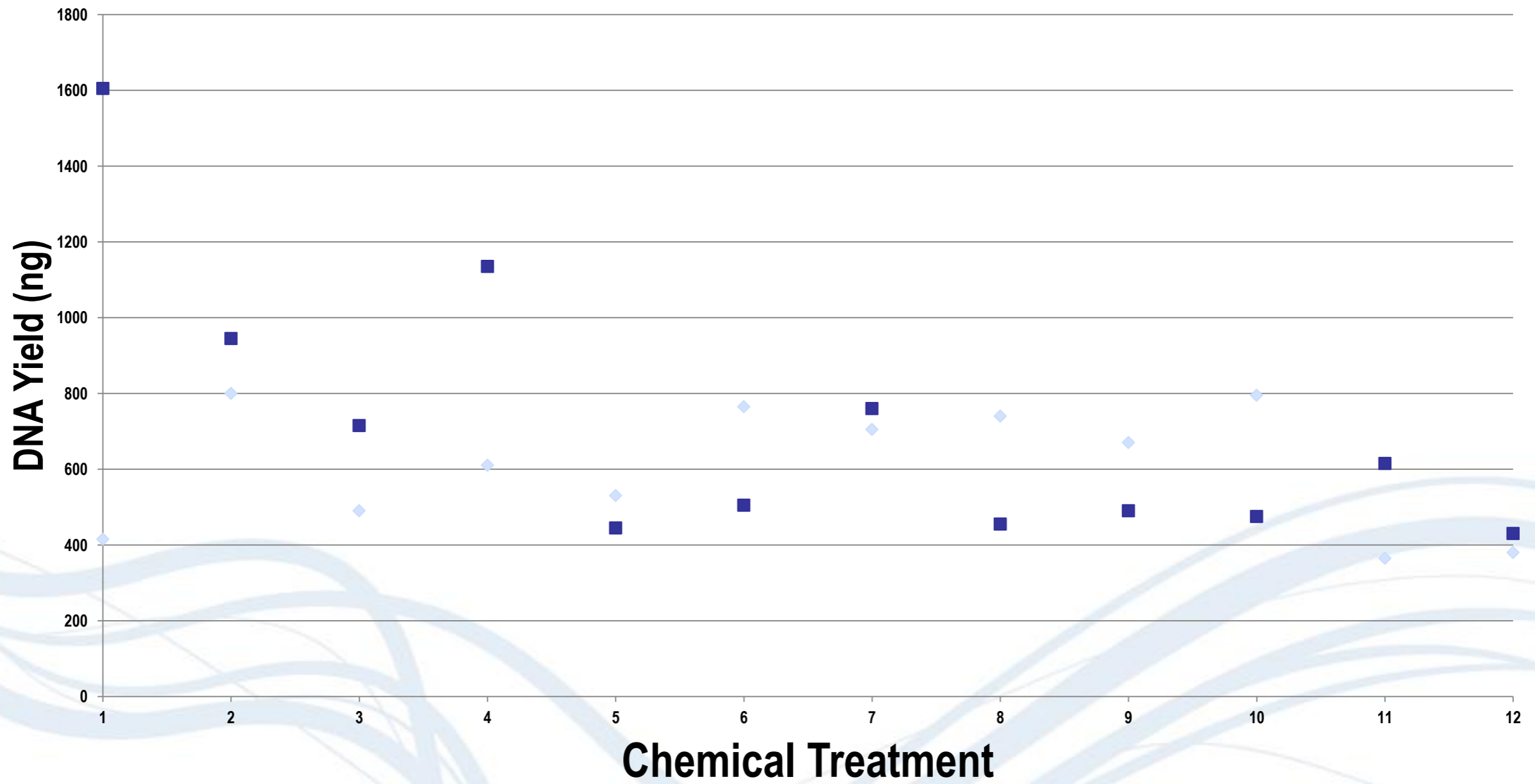
**Up to 2gr Desiccant**

# Chemical Treatment Optimization (Blood DNA)

- 200uL Matrix Wafers used for Screening
- Add 50uL of Bonding Agent-Stabilizer
- Add **50uL of Raw Blood**
- Air Dry with desiccant
- Apply 3-Day Extreme Heat Protocol:
  - 1 day 37C
  - 1 day 56C
  - 1 day 37C
- Rehydrate by adding 200uL H2O
- Purify DNA → Analyze

# Blood DNA Recovery: STD 3-Day Heat Protocol

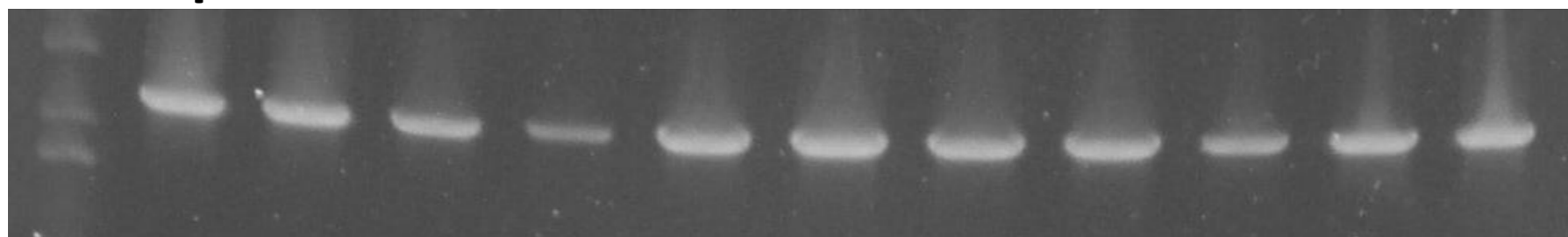
## DNA Yield from 50uL Whole Blood





# 2.4 kb “Long” mt-DNA QC Test

## MicroSphere Matrix



Lane	Top Row:	Bottom Row:
1	1 Kb DNA Extension Ladder (Invitrogen)	1 Kb DNA Extension Ladder (Invitrogen)
2	Roche Control DNA (100 pg)	Roche Control DNA (100 pg)
3	Roche Control DNA (50 pg)	Roche Control DNA (50 pg)
4	Roche Control DNA (25 pg)	Roche Control DNA (25 pg)
5	Blood Incubated w/o Matrix (100 pg)	Chemical Treatment 8 (100 pg)
6	Chemical Treatment 1 (100 pg)	Chemical Treatment 9 (100 pg)
7	Chemical Treatment 2 (100 pg)	Chemical Treatment 10 (100 pg)
8	Chemical Treatment 3 (100 pg)	Chemical Treatment 11 (100 pg)
9	Chemical Treatment 4 (100 pg)	Chemical Treatment 12 (100 pg)
10	Chemical Treatment 5 (100 pg)	Negative Control (not shown)
11	Chemical Treatment 6 (100 pg)	
12	Chemical Treatment 7 (100 pg)	

- **Multiple Matrix-Stabilizer Combinations Work for Blood DNA**
  - All Three Matrices
  - Ordinary DNA Purification (Qiagen)
  - >90% DNA recovery,  $A_{260}/A_{280} > 1.8$
  - DNA supports qPCR (no measurable inhibitors)
  - DNA intact to >2.4kb (Long mtDNA PCR)
- **In-Progress for DNA (March)**
  - More Rigorous Heat Test Model (2d@37C, 2d@56C, 2d@37C)
  - Pick Candidates to proceed to RNA & Protein

# Next Steps (April-June)

- **Design and Manufacture of Chaperone Prototypes**
  - Scale-up: Plastic Chaperone (5,000)
  - Scale-up: Aluminum Chaperones (5,000)
- **Stabilization Chemistry Optimization**
  - Blood RNA
  - Few Blood Proteins: IgA, IgG, IgM
  - Virus: Avian influenza virus (AIV) and exotic Newcastle disease virus (ENDV) Stabilization of Viral RNA and Host Igs

# Acknowledgements

- **DARPA            BAA-11-38 ADEPT: DxOD-PoC (2011)**  
**Matrix-Chaperone Materials Science Development**
  - Dennis Harris, D.Phil, Katy Metz, Lily Wong (IntegenX)
  
- **DHS                FAZD Center Grant (2011)**  
**Matrix-Chaperone Development for Viral Field Collection**
  - Tammy Beckham DVM, Ph.D, Dr Blanca Lupiani, PH.D (Texas A&M)
  - FAZD (Foreign Animal and Zoonic Disease, DHS National Center)
  
- **NCI                 R21 IMAT (2011)**  
**Apply Matrix Chemistry to “Natural” Porous Materials**  
**Stabilize DNA & RNA during Formalin Fixation**
  - Professor Margaret Gulley, MD
  - UNC Department Laboratory Medicine

# Matrix-Chaperone Questions & Comments???

**We are Actively Recruiting Collaborators for Summer (2012)**

- **Small Molecules, Metabolites, Cancer Biomarkers**

**Drs. Joshua Miller & Paul Luciw**

**Professors, Dept. Pathology & Laboratory Medicine, UC Davis**

- **Collection and Preservation of Live FMDV & Other Virus**

**Dr. Luis Rodriguez**

**Research Leader, Plum Island National Labs**

- **If you have Interesting Ideas, Samples, Biomarkers  
Please Contact Us to Discuss Collaboration**

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