

# Feasibility of delivering monoclonal antibodies in sexual lubricants: A novel delivery method for contraceptives

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## Background:

**Anti-sperm antibody:** Globally, 121 million unintended pregnancies occur every year and yet, male methods account for only 10% of contraceptive use. Currently, there are few contraception methods available for men: vasectomy, which is invasive, costly and not reliably reversible; and condoms and withdrawal, which are reversible methods but are associated with high failure rates (15% and 20% respectively). H6-3C4 is an IgM anti-sperm monoclonal antibody isolated from an infertile woman by Isojima *et al.*, in the 1980s. HCA is an IgG version of H6-3C4 made in *Nicotiana (N)* and binds to the male reproductive tract-specific glycoprotein CD52g which anchors on the sperm surface. This antibody potently agglutinates and immobilizes sperm. Our Phase I clinical trial using HCA vaginal film, ZB-06, is currently underway and preliminary results indicate that the film is safe and highly effective at immobilizing sperm in cervical mucus after intercourse. In this project we are evaluating the use of HCA in penile lubricants. This will be a novel way of transferring a potent contraception antibody from a man to his female partner during intercourse.

## Objectives

1. Evaluate the miscibility, compatibility and effectivity of HCA in various water and silicone-based sexual lubricants
2. Evaluate the stability over time and at various temperatures for HCA mixed with a lubricant
3. Assess the feasibility of delivering HCA using a “penile” application to “vaginal mucosa” in simulated intercourse

## Materials and Methods

Commercially available sexual lubricants: 5 water-based and 5 silicone-based lubricants were evaluated.

HCA was provided by ZabBio, Inc. (San Diego, CA).

A Fleshlight® and a cervical dilator were used as vaginal and penile simulators respectively.

Healthy men aged 18-45 years volunteered as semen donors.

### Processing of semen:

Semen was processed with 90% Isolete within one hour of receiving the sample, after liquefaction, to separate healthy motile sperm. Motile sperm were resuspended in Multipurpose Handling Media (MHM) at a concentration of 30 M/mL.

### Evaluation of HCA-lubricant (HCA+L) miscibility and sperm compatibility:

Lubricants were diluted 1:1 with MHM or HCA+MHM (final concentration 100µg/mL). Miscibility was determined by 2 observer visual evaluation. Sperm compatibility was assessed on the Computer Assisted Sperm Analyzer (CASA) as number of immotile sperm when added to the lubricant+MHM.

### Time and temperature stability:

HCA+L was stored at 4°C, Room temperature (RT) or 37°C over a 72-hour time course and HCA function was assessed at 24-hour intervals by the Kinetic Agglutination Assay by at least 2 observers.

### Simulated intercourse:

HCA (1mg/mL)+L mixture was applied to a “penis-like” object (i.e. vaginal dilator) and repeatedly inserted into a Fleshlight® (vaginal simulator) 10 times. After simulated intercourse, samples were obtained with Merocel swabs from the introitus (P1), vaginal canal (P2) and “cervical external os” (P3). Samples were eluted in PBS and stored overnight at 4° C. The concentration of HCA was determined using anti-sperm ELISA.

## Results:

Table 1: Evaluation of various lubricants and HCA mixtures:

ID#	Name	Type	Antibody Miscibility	Sperm Compatibility	HCA Agglutination (Kinetic Assay)
A	#LubeLife	Water-based	+	+	++
B	Astroglide Glycerin and Paraben Free	Water-based	+	-	+
C	Astroglide Water-based	Water-based	+	-	++
D	His & Hers Arousing and Tingling Personal Lubricant	Silicone-based	-	++	+
E	KY Jelly Classic	Water-based	-	+	+
F	KY True Feel Deluxe	Silicone-based	-	++	+++
G	Swiss Navy Silicone Lubricant	Silicone-based	+	++	+++
H	Trojan Lubricants Chain Reaction	Silicone-based	-	+++	++
I	Wet Platinum	Silicone-based	-	-	++
J	Wet Water-based	Water-based	-	-	+

**Sperm/Lube compatibility - Fold change of motile sperm in lube compared to media**

- 2+ fold change: +++
- 1-2 fold change: ++
- 0.5-1 fold change: +
- < 0.5 fold change: -

**HCA Agglutination (Kinetic Assay) - Time to 100% Agglutination**

- < 40 sec: +++
- 40-50 sec: ++
- 50-60 sec: +
- > 60 sec: -

Figure 1: HCA retains sperm agglutination function over 72 hours and over a range of temperature when mixed with Lubricant F

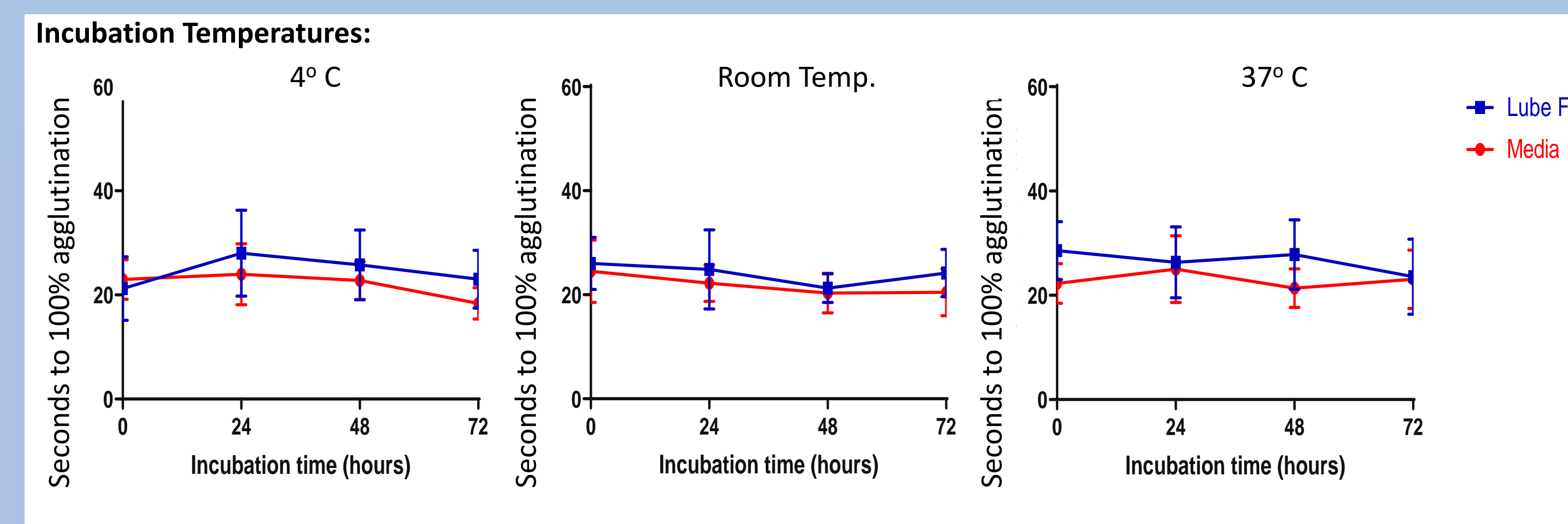


Figure 2: HCA retains sperm agglutination function in both water-based Lube A and silicone-based Lube F at HCA concentration ≥ 25µg/mL

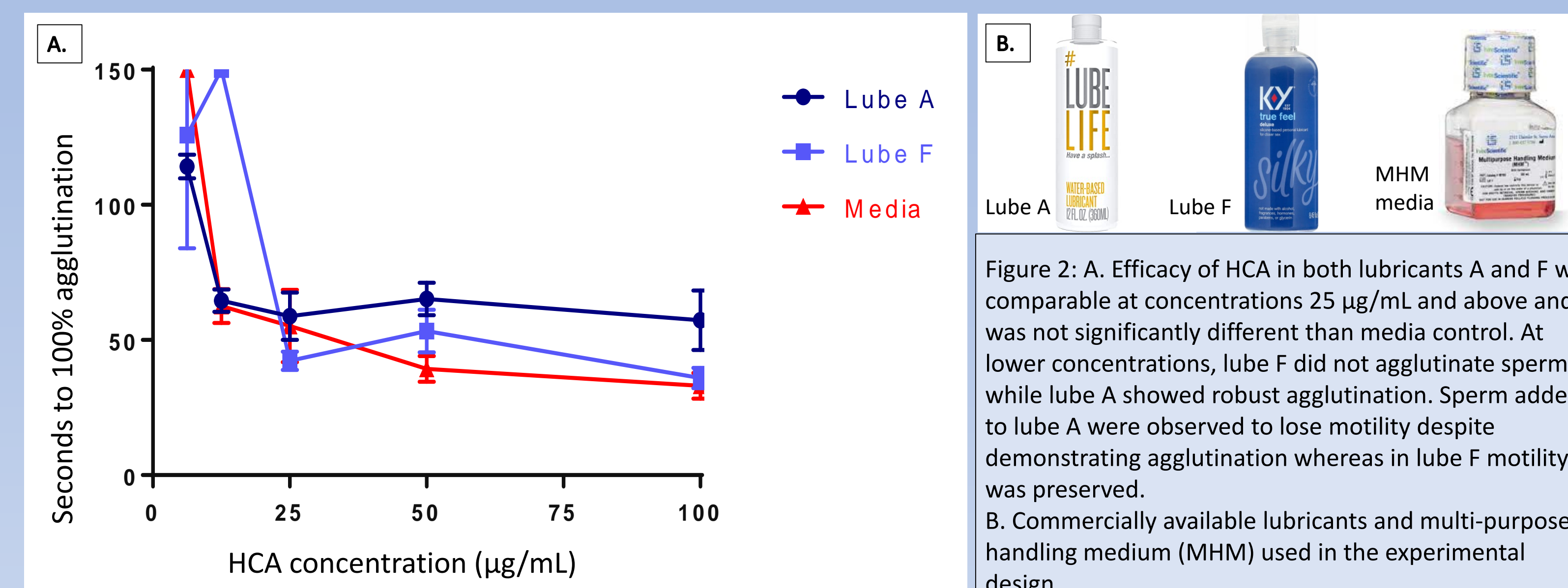


Figure 3: HCA can be delivered to the vagina via “penile” use of sexual lubricant at therapeutic doses needed for effective contraception.

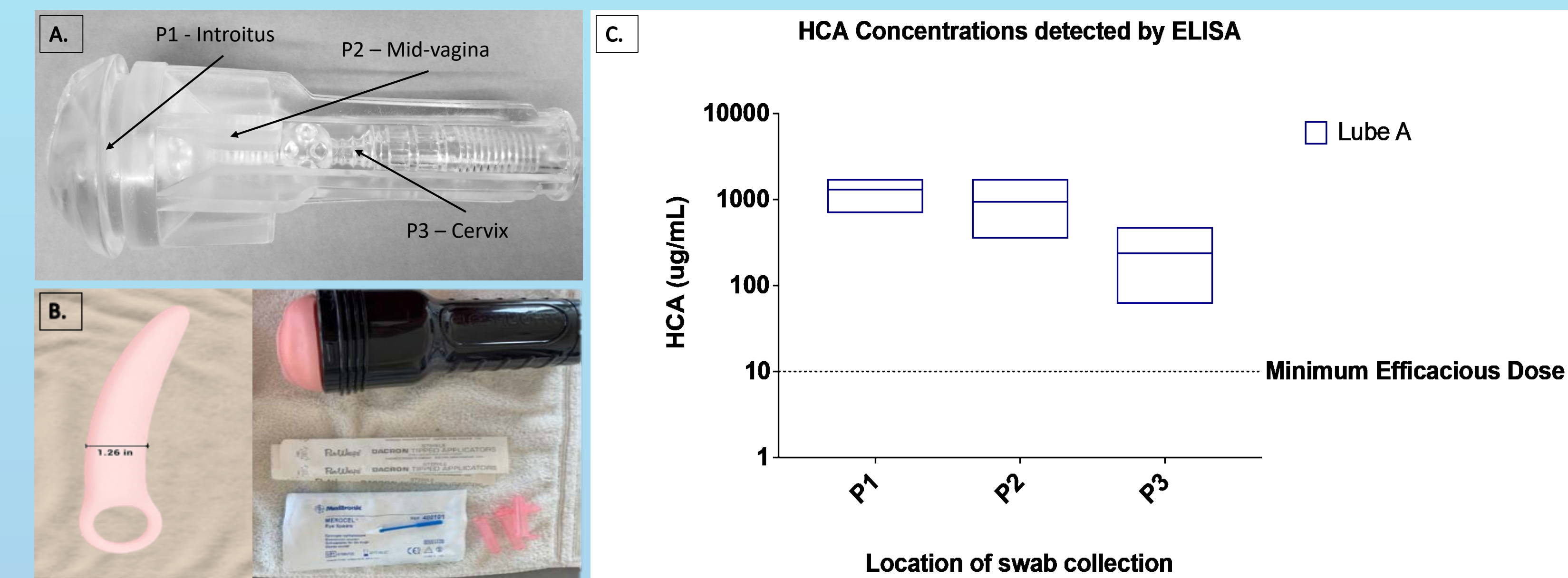


Figure 3: A. Fleshlight locations for sample acquisition post simulated intercourse. B. Experimental setup C. HCA concentrations from Merocel swab eluates from the “introitus”, “mid-vaginal” and “cervical external os” locations .

## Conclusions:

1. HCA mixed well with water-based sexual lubricants and formed an emulsion when mixed with silicone-based lubricants.
2. Lubricants alone had variable effects on sperm motility. Two of 5 water-based and 4 of 5 silicone-based lubricants caused significant reduction in sperm motility
3. Activity of HCA assessed by agglutination was variable but preserved in all lubricants tested.
4. HCA was stable in a silicone-based lubricant (ID# F) when stored for up to 72 hours at room temperature as well as 4 and 37°C. HCA-induced sperm agglutination was robust at 24, 48 and 72 hour time points.
5. Preliminary data suggests that HCA can be delivered via sexual lubricant use during simulated intercourse and in doses significantly above the threshold needed to achieve effective contraception.

Together these preliminary findings suggest that use of HCA in penile lubricants will be a novel way of transferring a potent contraception antibody from the penile surface to vaginal mucosa during intercourse.

## References:

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