Choosing Prevention: The Case for Involving Users in Early Microbicide Development

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ACKNOWLEDGEMENTS

NIH Microbicide Innovation Program

Project LINK

NIH/NIMH R21/R33 MH80591 & CONRAD/USAID PPA-09-0223

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FCHC team: L Salomon, K Mayer, D Perry, L Panther, C Covahey, D Dang, M Gelman, V Frontiero

Donations of Study Products and Materials from:
CONRAD, HTI Plastics, Good for Her, Rip n Roll
GOALS

- Make the case for a user-centered approach to product development in HIV prevention
- Introduce a new element of understanding factors related to acceptability and adherence: “Perceptibility”
- Provide initial data in support of integrating perceptibility into biomedical prevention technology development
Microbicides – or any biomedical prevention products – need to be used to be effective

Effectiveness is dependent on both biologic efficacy and user behavior

Biologic efficacy is dependent on drug(s)... and drug delivery to, and retention in, target tissues

Drug delivery – with respect to vaginal and/or rectal products - is dependent on rheological and other biophysical properties of drug delivery systems
  + Formulations: e.g., gels, films, etc

What’s a “rheological or other biophysical property”?...
Viscosity, yield stress at various shear rates, viscoelasticity… the “feel” and “flow” of semi-solid formulations.
What if it turns out that formulation properties (like the ones that govern drug delivery) also govern user behavior...?

- A *non*-optimized user experience will ultimately negate an optimized drug and its delivery (or lack thereof)

- Need to balance optimization of drug delivery with optimization of the user experience
Perceptibility: The objective measurement of user sensory perceptions and experiences (USPE) of formulation and/or device characteristics and their performance during use.

Distinct from conventional “acceptability” and “tolerability”

But... perhaps a precursor to both
MEASURING WHAT...?

- Sensations of form, pressure, distortion, slip, texture, etc...:
  + “Feel”: lubricity, smooth, tacky, dry, slick, oily, sticky, wet, moist, thick/thin, liquidy, drippy, stringy... etc.
  + Pressure and Movement: physical awareness, fullness, “foreign object,” messiness, leakage
  + Changes in USPE over time: during application/insertion, during ambulation, at initial penetration, early intercourse, end of intercourse, “average” over time
    - Changes in viscosity, pressure, temperature, and feel
User-Identified Gel Characteristics: A Qualitative Exploration of Perceived Product Efficacy of Topical Vaginal Microbicides

Kathleen M. Morrow · Kristen Underhill · Jacob J. van den Berg · Sara Vargas · Rochelle K. Rosen · David F. Katz

“Set it and Forget it”: Women’s Perceptions and Opinions of Long-Acting Topical Vaginal Gels

Jacob J. van den Berg · Rochelle K. Rosen · Dana E. Bregman · Lara A. Thompson · Kathleen M. Jensen · Patrick F. Kiser · David F. Katz · Karen Buckheit · Robert W. Buckheit Jr. · Kathleen M. Morrow

Designing Preclinical Perceptibility Measures to Evaluate Topical Vaginal Gel Formulations: Relating User Sensory Perceptions and Experiences to Formulation Properties

Kathleen M. Morrow,1,2 Joseph L. Fava,1 Rochelle K. Rosen,1,3 Sara Vargas,1,2 Julia G. Shaw,1 E. Milu Kojic,4,5 Patrick F. Kiser,5 David R. Friend,7 David F. Katz,8 and The Project LINK Study Team
PROJECT LINK: THE MAKING OF USPE SCALES

**in mano Experience**

**Application Experience**

**Ambulation Experience**

**Sexual Experience**

- **Qual IDIs**
  - Stage 1: n=16, IDI k=32, Cog k=16

- **Cognitive Interview**
  - 2 products

- **in mano scales**
  - Stage 2 n=121

- **Application scales**
  - Stage 3 n=204

- **Ambulation scales**

- **Sex scales**

- 4 novel formulations
## Link Formulations

<table>
<thead>
<tr>
<th>Gel Primary Composition</th>
<th>3% HEC</th>
<th>1.25% Carbopol</th>
<th>3% HEC; 2.5% Carbopol</th>
<th>2% HEC; 1.73% Carbopol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Undiluted</td>
<td>Diluted</td>
<td>Undiluted</td>
<td>Diluted</td>
</tr>
<tr>
<td>Viscosity at 1s (pa-s)</td>
<td>96</td>
<td>40</td>
<td>250</td>
<td>184</td>
</tr>
<tr>
<td>Residual Stress (Pa)</td>
<td>13</td>
<td>0</td>
<td>129</td>
<td>87</td>
</tr>
<tr>
<td>Volume (mL)</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Area Coated at 2.5 min (cm²)</td>
<td>53</td>
<td>67</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Area Coated at 6 min (cm²)</td>
<td>57</td>
<td>76</td>
<td>35</td>
<td>36</td>
</tr>
</tbody>
</table>

* Diluted with 20% Vaginal Fluid Simulant
FIG. 3. Perceptibility Scales for Sexual Activity.

Figure 3. Averaged scale item scores for each Perceptibility Scale for Sexual Activity. 1=do not agree at all; 2=agree a little; 3=agree somewhat; 4= agree a lot; and 5= agree completely. Primary constituents for each gel were: 3% hydroxyethylcellulose (HEC) (orange); 1.25% carbopol (yellow); 2% HEC and 1.73% carbopol (purple); and 3% HEC and 2.5% carbopol (green). Pair-wise comparisons are presented in Table 6.
So...

- Women can feel things in their vaginas.
- Women can discriminate one product from another product with respect to the way those products “feel” and “behave” in their bodies.
- But women don’t have discrete scale-by-scale sensations … they have experiences…
No single gel was preferred:

- 34% chose Orange [low viscosity, low residual stress];
- 15% chose Green [high viscosity, high residual stress];
- 51% chose 1 of 2 gels w/more complicated profiles:
  - Purple (26%)
  - Yellow (25%)

So... if a specific gel isn’t chosen then what is...?
CHOICE-EXPERIENCE PATTERNS

Class 1: 14%
Class 2: 28%
Class 3: 25%
Class 4: 33%

Averaged Scale Item Score

Initial Penetration
Initial Lubrication
Intravaginal Awareness
Perceived Wetness
Stimulating
Messiness
Perceived Leakage
"THE SWEET SPOT"

Target Product Perceptibility

Averaged Scale Item Score

- Initial Penetration
- Initial Lubrication
- Intravaginal Awareness
- Perceived Wetness
- Stimulating
- Messiness
- Perceived Leakage
**BETWEEN CLASS DIFFERENCES**

<table>
<thead>
<tr>
<th></th>
<th>Class 1</th>
<th>Class 2</th>
<th>Class 3</th>
<th>Class 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.8 (7.5)</td>
<td>29.7 (8.6)</td>
<td>27.7 (7.9)</td>
<td>29.0 (7.7)</td>
</tr>
<tr>
<td>Race (% Caucasian)</td>
<td>57.1%</td>
<td>42.6%</td>
<td>50.0%</td>
<td>65.2%</td>
</tr>
<tr>
<td>Ethnicity (% Non-Hispanic/Non-Latino)</td>
<td>82.1%</td>
<td>83.6%</td>
<td>84.8%</td>
<td>88.4%</td>
</tr>
<tr>
<td>Income (%&gt;36k)</td>
<td>25.0%</td>
<td>25.0%</td>
<td>24.4%</td>
<td>34.8%</td>
</tr>
<tr>
<td>Vaginal Deliveries (% None)</td>
<td>64.3%</td>
<td>62.3%</td>
<td>71.7%</td>
<td>69.6%</td>
</tr>
<tr>
<td>Current Use of Hormonal Contraceptive (%)</td>
<td>28.6%</td>
<td>27.9%</td>
<td>43.5%</td>
<td>37.7%</td>
</tr>
<tr>
<td>History of STD Infection</td>
<td>21.4%</td>
<td>20.0%</td>
<td>17.8%</td>
<td>18.8%</td>
</tr>
</tbody>
</table>

*p<0.05 for between-class difference

... neither sociodemographics nor behavioral history differentiated classes of choice-experience patterns
WHAT DO USERS WANT?

- There is no one answer
- The scale most correlated with class is Initial Penetration.
  - If all the scales are put into the model to predict class, the most associated is **Initial Penetration**: thus Initial Penetration, in this parameter space, is **most predictive of choice experience**.
  - The next two most correlated with class (which is determined by choice product) are Intravaginal Awareness and Perceived Wetness
- What does this mean? (educated guess)
  - It’s important that a product provide the “best” initial penetration experience (whichever way they like it); that their awareness of it conveys the “right” message; and that they feel as much like “normal” as possible
The LINK data only applies to a gel parameter space - and a limited one at that

+ We are currently conducting analyses for vaginal films and suppositories
+ We have not yet psychometrically validated similar USPE constructs for intravaginal ring use
CONCLUSION-1

- Microbicide effectiveness is predicated on optimal drug delivery AND optimal use adherence.
- Both drug delivery (and resulting efficacy) - and use are impacted by rheological and other biophysical properties of gel formulations.
- Clinical trials have been challenged by low adherence, obviating proof of concept.
CONCLUSION-2

- If we can understand the correspondence between product properties and the user experience elicited by those properties, we can:
  + Develop products that meet a defined set of parameters most likely to “hit the sweet spot”
  + Develop educational materials or behavioral interventions that help users “cope” with use sensations and experiences that cannot be changed due to their impact on efficacy
  + Make products people will use, increasing the likelihood of improved adherence and impact on HIV incidence.
THANK YOU!!

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