Let's Talk MPTs

MPT Regulatory Pathways: Case Studies From MPT Product Developers

Speakers include: Mary Weitzel, Daniel Loeven & Wilberto Robles

Monday, 28 February at 07:30 PT/10:30 ET/15:30 GMT/17:30 CEST/17:30 SAST/18:30 EAT

Webinar Registration Link: bit.ly/IMPTregFEB2022

Welcome! All participants will be muted during the presentation and discussion. Please use the chat for questions.

During the Q&A, please unmute for a question or comment, and mute if you are not speaking. Thank you!
Let’s Talk MPTs Discussion Series
28 February 2022

Webinar Agenda

- Welcome & Introductions
- Presentations
  - Reproductive Health Drug Products: Regulatory and Development Perspective by Mary Weitzel (Yaso Therapeutics)
  - MPT Regulatory Pathways and Challenges by Daniel Loeven (Population Council)
  - Global Regulatory Considerations & Five Secrets for Success! by Wilberto Robles (WCG Cares)
- Facilitated discussion
- Wrap Up & Adjourn
Multipurpose Prevention Technologies

**MPTs combine protection against:**
- Unintended pregnancy
- HIV
- Other STIs

**MPTs have the potential to:**
- Address overlapping risks
- Synergize prevention approaches
- Increase motivation for adherence
- Destigmatize HIV prevention
- Improve health & economic outcomes
What is the *Let’s Talk MPTs* Discussion Series?

- A platform aimed to engage experts from diverse disciplines across the globe to help address MPT and HIV prevention R&D priorities and gaps

- Past topics include:

- Recordings and upcoming webinars available at [theIMPT.org](http://theIMPT.org)
Today’s Discussants

Mary Weitzel, MBA

Daniel Loeven, MS

Wilberto Robles, MCC, MTOPRA
To: IMPT

Mary Weitzel – co-founder, President, CEO, PI
February 28, 2022
Goal: Vaginal gel for contraception and STI prevention

Considerations

- **FDA is not structured to consider simultaneous indications using a single New Chemical Entity (NCE)**
  - **Solution**: Meet with each division of FDA with authority over the claim
  - Developed preclinical plans with current subject matter experts in CMC, safety toxicology and vaginal microbicides and reviewed Guidance to Industry docs
  - Presented preclinical studies plan to both divisions. (Div. of Anti Viral Products and Div. of Bone Reproductive and Urinary Products.)
  - Feedback combined into a single plan (no major conflicts found)

- **Reduced Cost and Time Advantages:**
  - Preclinical toxicology applies to all indications
  - PD/PK Applicable to all indications for single Route of Administration
  - **A single Phase 1 clinical trial may be sufficient to support multiple Phase 2 clinical trials**
Phase II/III clinical trials

Considerations

- **Phased clinical trials for each indication**
  - Clear endpoints
  - Identifiable special populations
  - Focused, faster clinical trials
  - Select indications based on urgency, fundability, minimal time to Phase III trial
  - Maintain patent life

- **Benefits of single NCE**
  - Efficient use of capital
  - Reduce cost of goods (COGS)
  - PD/PK Applicable to all indications for single Route of Administration
Our goal: **Single gel with multiple indications**

- **Contraception**
  - Phase I
  - Phase II
  - Phase III NDA

- **Herpes Treatment/Prevention**
  - Ph IIa/Ph IIb
  - Phase III NDA

- **Gc/Ct Prevention**
  - Ph II
  - Phase III NDA

- **HIV – gel & film**

- ✓ Maintain and generate new IP
- ✓ Time to market
- ✓ Strike partnerships
- ✓ Out license

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Regulatory Terms for Yaso Gel

- **NCE = “Drug Substance”**
  - **Issue:** Substantially more CMC and safety toxicology studies required than if repurposing an already approved drug. More money, more time

- **Gel = “Drug Product”**
  - Use only currently FDA approved excipients at ≤ concentration per route of administration
  - Use only a CRO/CMO with substantial, current experience with your dosage form
  - Less money and time required to use a single gel for multiple indications

- **Finished good product “Combination Product”**
  - Vaginal applicators are considered a Class 1 medical device thus final product is a combination of a drug product and a medical device. The gel and the appropriate division will (most likely) run the regulatory review process. Seek low cost, biodegradable applicator, if possible.
  - Stability is important. Examples of risks: moisture loss, leakage from the applicator, impact on the waste stream in the local environment, compatibility
Approach Tips

- Become familiar with and adopt Quality by Design (QdB), as described by FDA, ASAP when tackling Preclinical/ PreIND studies

- Early Type B meeting with appropriate division of FDA is a must – do not rely on history and don’t wait until you are ready to submit an IND

- Involve CURRENT pharmaceutical commercial and regulatory experts in addition to the experts on your technology and the field

- Adopt Design of Experiments (DOE, Taguchi, etc.) to optimize a gel or combination product, if possible

- Define early, and rigorously follow, Vendor selection policies and procedures
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- Charles River Laboratories
- Wilmington Pharmatech
- Bioreliance
- Dow Development Laboratories
- FDA Division of Anti Viral Products
- FDA Division of Urology, Obstetrics and Gynecology
FDA GUIDANCE FOR INDUSTRY DOCUMENTS – A SELECTION

- Quality Systems Approach to Pharmaceutical CGMP Regulations
- Anti-Viral Product Development – Conducting and Submitting Virology Studies to the Agency
- Bioanalytical Method Validation – Draft guidance
- Current Good Manufacturing Practice Requirements for Combination Products
- Common Technical Document (CTD) from International Conference on Harmonization (ICH)
- M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorizations for Pharmaceuticals
- M4, all should be reviewed – all efficacy, safety and quality
- Q1A – Stability Testing of New Drug Substances and Products
- Guidance for Development of Vaginal Contraceptive Drugs – 1995
- Vaginal Microbicides Development for the Prevention of HIV Infection
IMPT WEBINAR ON REGULATORY PATHWAYS AND CHALLENGES

Daniel Loeven
Director, Global Regulatory Affairs and Quality Assurance

February 28, 2022
Select Council MPT Products: HIV and Contraception

- Etonogestrel/Ethinyl Estradiol/QGriffithsin Pod Ring
  - EEQ

- Griffithsin/Carrageenan Fast Dissolving Insert
  - FDI

- Dual Prevention Pill: DPP

- PrEP (Pre-exposure prophylaxis)
MPT Pathway: A Typology

**INDICATION COMBINATION**
- **DPP**
  - Pregnancy + HIV
- **FDI**
  - STIs + HIV
- **EEQ**
  - Pregnancy + STIs + HIV

**FORMULATION/DELIVERY VEHICLE**
- **DPP**
  - DRUG + DRUG
- **FDI**
  - DRUG + DEVICE
- **EEQ**
  - DRUG + DEVICE

**ACTIVE PHARMACEUTICAL INGREDIENT (API)/DEVICE STATUS**
- **DPP**
  - APPROVED + APPROVED
- **EEQ**
  - APPROVED + EXPERIMENTAL
- **FDI**
  - EXPERIMENTAL + EXPERIMENTAL

**REGULATORY PATHWAY**
# OF INDICATIONS + # OF API/DRUG ~ # YEARS

Martha Brady
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Regulatory Challenges

• The combination rule
• Clinical efficacy for each indication (how to prioritize?)
• Combining labeling for contraceptives and other drugs
• MPT’s often have a device that is a constituent part
• CMC (Chemistry Manufacturing and Control) issues of analytical complexity
Combination Rule

Two or more drugs may be combined in a single dosage form when:

- each component contributes to the claimed effects and the dosage of each component (amount, frequency, duration)
- the combination is safe and effective
- a significant patient population requires concurrent therapy
New Guidance on Combination Products

Principles of Premarket Pathways for Combination Products - January 2022

Guidance covers which FDA center will be the lead reviewer

If there is a drug device combination, the lead reviewing center will be based on which constituent part provides the primary mode of action (PMOA) of the combination product.
There are no shortcuts for labeling

- Labeling is an important part of the submission needed for approval
- For MPTs where often we are combining products, some of which have existing approved labeling
- DPP is composed of 4 FDA approved drugs (2 products: oral contraceptive and PrEP)
  - Proposed using the two approved labels to FDA
  - FDA said no – we must write a new, integrated label
MPTs often have a Device that is a constituent part, which can lead to additional requirements

- Risk Analysis
- Design verification
- dFMEA - device failure mode and effects analysis
- Biocompatibility of the product
- Mechanical testing, and stability of mechanic properties
- Condom compatibility
- Fate of Implant
Chemistry Manufacturing and Control (CMC) Issues

• Additional testing required for device constituent part
• Complexity of analytical procedures increases with multiple actives
The Population Council conducts research and delivers solutions that improve lives around the world. Big ideas supported by evidence: It’s our model for global change.
Global Regulatory Considerations & Five Secrets for Success!

Wilberto Robles, Sr. Director, Global Regulatory Affairs & Quality Assurance

WCG Cares

February 2022
Why does registration matter?

• Regulatory authorities protect public health by ensuring:
  • Safety
  • Efficacy
  • Quality
Of drugs, medical devices, and other regulated products
Who regulates?

National Regulatory Authority (NRA)

- Responsible for reviewing and granting or rejecting registration applications in the countries where they have the legal authority to do so.
- ZAMRA, NAFDAC, DPM

Stringent Regulatory Authority (SRA)

- Provide expertise and resources for the proper evaluation of regulated products.
- US FDA, EMA, Japan, Health Canada
Product Classification Categories for Regulatory Application

- **Medical device**
  - Examples: diaphragms, condoms

- **Combination product**
  - Example: levonorgestrel intrauterine system in some countries

- **Drug product or medicine**
  - Examples: oral contraceptive pills
Registration Dossiers

Common Technical Document (CTD)

Technical File or Design Dossier
Registration Pathways - Country-by-Country Registrations
Registration Pathways - Regional Harmonization Initiatives
Registration Pathways - World Health Organization

- Supports access to essential medicines
- Sets norms, standards, develops guidelines
- Advises on issues related to quality assurance
- Assists in building national regulatory capacity
- Prequalification Programme
Registration Pathways - Special Import Permits

• Short-term use
  • Research
  • Emergencies

• Application guidelines, and willingness to approve special import permits, are country-specific
So, which pathway to choose?

Do you intend to register the product in multiple countries?
- Yes
  - Has the product received WHO PQ or approval from an SRA?
    - Yes
      - Consider applying for full WHO PQ to enable use of the WHO Collaborative Procedure.
    - No
      - Your product may be eligible for accelerated registration, which can be a cost-effective option resulting in expedited approval at the country level.
      - See WHO’s “Collaborative Procedures for Accelerated Registration.”
  - No
    - Do you have the time and resources to apply for full WHO PQ?
      - Yes
        - Consider leveraging regional harmonization. Some regions* currently offer standardized guidelines and expedited review, which can accelerate national registrations.
        - *EAC, ZAIBONA, and CARICOM as of 2018
      - No
        - PURSUE NATIONAL-LEVEL REGISTRATION.
        - The national registration process will be faster and simpler if the product has prior approval from a regional platform or WHO Collaborative Procedure.

Are 2+ of the countries in the same region?
- Yes
  - Consider leveraging regional harmonization. Some regions* currently offer standardized guidelines and expedited review, which can accelerate national registrations.
  - No
    - PURSUE NATIONAL-LEVEL REGISTRATION.
    - The national registration process will be faster and simpler if the product has prior approval from a regional platform or WHO Collaborative Procedure.
Product Registration Steps

1. Conduct a desktop assessment to review country-specific registration requirements available online and to identify local stakeholders and potential MAH candidates.
2. Perform an in-country regulatory landscape assessment (if needed).
3. Assist the manufacturer or sponsor to select and appoint an MAH.
4. Communicate with the manufacturer to obtain required documents for registration.
5. Submit registration dossier on behalf of manufacturer.
6. Request import permit for any samples needed as part of the registration process.
7. Upon receipt of import permit, coordinate shipment of samples from manufacturer to regulatory authorities in country.
8. Communicate receipt of marketing authorization letter with internal and external partners.
9. Prepare requests for post-registration updates as the need arises.
Five Secrets for Success!
SECRET #1

Make Sure You Understand The Regulatory Landscape And Identify The Right Registration Pathway For Your Product
SECRET #2

Identify A Good Local Partner
SECRET #3

Meet The Local Authorities
And Stakeholders
SECRET #4

Establish Good Post-approval Registration Management
SECRET #5

Keep Calm And Don’t Panic...
Success always takes help. Failure is done alone.

-Simon Sinek
Thank you

Wilberto Robles
Sr. Director, Global Regulatory Affairs & Quality Assurance
+1.787.405.2064
wrobles@wcgcares.org
http://www.wcgcares.org/
Q&A

- Please submit questions to the chat
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Thank You!