WEBINAR
Harmonized Labeling for the Hormonal IUD in Low- and Middle-Income Countries
March 22, 2022, 7am PT / 10am ET
Agenda

- Welcome
- What is “Harmonized Labeling” and Why is it Important?
- Overview: The Hormonal IUD and Avibela
- The Case for Harmonized Labeling & Key Challenges to Harmonization
- Project Activities
- Key Findings
- Avibela Labeling Harmonization Strategy
- Q&A
Poll #1

• How do you define your organization?
  1. Pharmaceutical manufacturer and/or distributor
  2. Procurement agency
  3. Donor
  4. Government (MOH, NMRA)
  5. Service Delivery Organization (NGO/SMO)
  6. Regulatory Agency/Consultancy
  7. Other
What is “Harmonized Labeling” and Why is it important?

Harmonized labeling refers to the use of identical product labeling across multiple countries.

Harmonized labeling can create time and cost efficiencies that benefit stakeholders across the value chain.
The Hormonal IUD in LMICs

1990
Hormonal IUD first approved in Finland (Mirena®)

Bayer AG and Population Council establish the International Contraceptive Access Foundation (ICA Foundation) to provide local service-delivery organizations with the hormonal IUD on a not-for-profit basis, primarily in developing countries

2003
U.S. FDA approval of Medicines360’s hormonal IUD; Medicines360 offers deeply discounted price for LMICs

2015
WHO adds method to model Essential Medicines List; releases Expression of Interest for PQ
USAID establishes global hormonal IUD working group and initiates global learning agenda

2018
Preliminary results from pilot projects published; additional publications continue through 2021, showing unmet need for the method and high user satisfaction and continuation rates

2020
Hormonal IUD Access Group launches to support scale-up of method; develops global forecast

2021
Hormonal IUD (including Avibela) added to USAID and UNFPA product catalogs
M360 announces Avibela price subsidy for global procurement agencies through 2024
History of Impact RH360 and Avibela

Medicines 360

founded to bring an affordable IUD to market in the U.S.

IMPACT RH360

formed to expand access to women in low- and middle-income countries

Avibela

(levonorgestrel-releasing intrauterine system) 52 mg

approved in Kenya and Nigeria

Avibela approved in Madagascar and Zambia

FDA approval of Liletta for 6 years of use

FDA approval of Liletta for 5 years of use

FDA approval of Liletta for 4 years of use

FDA approval of Liletta for 3 years of use

2009

2014

2015

2017

2018

2019

2021

*East African Community Medicines Regulatory Harmonization program
Select Current and Pending Avibela Registrations

- Registered
- Pending Registration

Avibela®
(levonorgestrel-releasing intrauterine system) 52 mg

Nigeria
Zambia
Uganda
Rwanda
Kenya
Tanzania
Madagascar
The Case for Harmonized Labeling

- Shorter lead times for producing and supplying product
- Reduction in human & material resource requirements for label creation, printing, and packaging
- More supply chain flexibility: the same stock can be deployed to numerous destinations
- Decreased risk of labeling inconsistency and errors
- Less wastage of packaging
Key Challenges to Harmonization

- Lack of publicly available information
- Requirements for country-specific information
- Approval timelines for labeling variations can be lengthy
Poll #2

What comprises regulated product “labeling”? Please select all that apply.
1. Primary packaging (e.g., pouch)
2. Secondary packaging (e.g., unit carton)
3. Summary of Product Characteristics and Prescribing Information
4. Patient Information Leaflet
Non-Harmonized Labeling: Madagascar

Pouch Label
Non-Harmonized Labeling: Madagascar

Summary of Product Characteristics and Prescribing Information

Country specific information

Country specific information
Non-Harmonized Labeling: Madagascar

Patient Information Leaflet

Country specific information
Non-Harmonized Labeling: Madagascar

Unit Carton

Country specific information
Project Activities

- Desk Review
- Stakeholder Interviews
- Labeling Development
1. Some level of harmonization is possible for the majority of countries assessed.

2. Manufacturers generally do not believe there is an advantage to proactive engagement with regulators about labeling guidelines.

3. While procurement agencies prefer multi-language labeling, other products with single-language labeling have been procured in large volumes.

4. Approved harmonized labeling of similar products differs from guidelines published by regulators.

5. A clear value proposition is critical: regulators are more willing to make allowances for products that are readily available, inexpensive, and respond to critical health needs.

6. Global contact information for pharmacovigilance reporting appears to acceptable to regulators and procurers.
## Labeling Component Requirements

<table>
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<tr>
<th>Component</th>
<th>Country-Specific Variable Information Required</th>
<th>Languages Required in 21 Countries Assessed</th>
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| **Pouch Label**         | Marketing Authorization Holder (MAH) name and address, local registration number, registration number in the country of origin, scheduling status, requirement for “generic name to be more prominent on the label than trade name” | • Afrikaans³ (South Africa)  
• Bahasa (Malaysia)  
• English – 13 countries  
• French – 5 countries  
• Vietnamese (Vietnam) |
| **Summary of Product Characteristics** | MAH name and address, contact info for AE reporting, registration number, scheduling status, date of first authorization & renewal. Note: format requirements also vary slightly | • Afrikaans³ (South Africa)  
• English – 14 countries  
• French – 5 countries  
• Vietnamese (Vietnam) |
| **Patient Information Leaflet** | Local registration number, scheduling status. Note: required format also varies slightly | • Afrikaans³ (South Africa)  
• Bahasa (Malaysia)  
• English – 12 countries  
• French – 5 countries  
• Sinhala, Tamil (Sri Lanka)  
• Vietnamese (Vietnam) |
| **Unit Carton**         | MAH name & address, and local registration number                                                              | • Afrikaans³ (South Africa)  
• English – 14 countries  
• French – 5 countries  
• Vietnamese (Vietnam) |

1 Or any of South Africa’s other 12 local languages
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<th><strong>Interview Findings</strong></th>
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| **Harmonized labeling is preferred by procurers and manufacturers** | Increases efficiency by reducing lead time and costs |
| **Achieving and maintaining harmonized labeling is complex and resource-intensive** | “Over-harmonization” can result in diminishing returns |
| **Manufacturers do not believe there is an advantage to proactive engagement with NMRAs** | A strong value proposition is required to advance regulatory approval of harmonized labeling |
| **Some country-specific requirements exist to reduce the risk of fraudulent/diverted product** | This risk must be considered in harmonization efforts |
| **PV reporting contact info does not represent a significant barrier to harmonization** | There is already precedent for the acceptability of global contact info |
| **WHO PQ of products is helpful for harmonization** | Local regulatory agencies generally accept standard labeling approved by WHO |
Avibela Labeling Harmonization Plan

Short-Term

*Single Language Labeling*

- Does not require the manufacturer to validate new labeling sizes
- Allows Avibela to achieve some level of harmonization in the relative short-term

Long-Term

*Potential for multi-language labeling*

- Requires redesign of the artwork and validation of new labeling sizes for some components
- To be aligned with future label changes
- Potentially allows Avibela to achieve further harmonization
Result

Fewer unique labeling components

Current State

• Madagascar, Kenya, Zambia, and Nigeria EACH have four unique labeling components
• Total = 16 unique labeling components across four markets

Harmonized Future State

• Madagascar has four labeling components (to be shared across future francophone countries)
• Kenya, Zambia, and Nigeria share the same four labeling components
• Total = 8 unique labeling components across four markets
Harmonized Labeling
Pharmacovigilance Reporting Information

Contact Information for Reporting of Adverse Events

**Kenya**

Marie Stopes Kenya
Kinderuma Road, Off Ngong Road
Kilimani, Nairobi
Phone: 0800 720 005 / 254 (0) 57 252 3 218
Email: info@mariestopese.or.ke

The Pharmacy and Poison Board
Lenana Road
Nairobi
Phone: (020) 2716805/6 ext 114
Email: pv@pharmacyboardkenya.org

**Madagascar**

PSI Madagascar
Immeuble ARBORETUM
Ex village des Jeux ANKordonDrano
ANTANANARIVO 101
Phone: + 261-20-22-629-84

Le Centre National de Pharmacovigilance de Madagascar
– CNPV
Phone: 20 22 395 22 ext. 301
Harmonized English

- Pouch Label and Directional Sticker

- Removed distributor information
- Removed product registration numbers
Harmonized English

Patient Information Leaflet

Removed in-country distributor information and left manufacturer and MAH information:

Manufactured by:
Odyssea Pharma SPRL
Rue du Travail, 16
B-4460
Grâce-Hollogne, Belgium

Manufactured for
Impact RH360 LLC
49 Stevenson St. Ste. 1100
San Francisco, CA 94105

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AVIBELA® is a trademark of Medicines360.

Removed local PV contact info and replaced with guidance for patient to contact HCPs about side effects:

**Reporting of side effects**
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your healthcare provider.
Harmonized English

Summary of Product Characteristics

7. SUPPLIER AND MANUFACTURER

Supplied by:
Impact RH360 LLC
49 Stevenson St., Suite 1100
San Francisco, CA 94105
Telephone: 1-415-951-8700

Manufactured by:
Odyssea Pharma SPRL
Rue du Travail, 16
B-4460
Grâce-Hollogne, Belgium

Removed distributor information

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system or to the local partner. Patients are encouraged to call their healthcare provider if they have any concerns about AVIBELA and patients may also report any suspected adverse reactions via the national reporting system or to the local partner. Contact information for the national reporting systems and local partners can be found at www.avibelapv.com.

Removed local PV contact info and added global URL and QR code
Added all current product registration numbers (instead of listing only a few on pouch label)

Removed local distributor information
Next Steps

- Post-approval variations
- New filings
Project Team

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FHI 360
Thank you

- AbbVie Inc
- Bill & Melinda Gates Foundation
- DDReg Pharma Regulatory Solutions
- FHI 360
- Gynuity Health Projects
- International Planned Parenthood Federation
- Organon
- Partnership for Supply Chain Management
- Zwiers Regulatory Consultancy
Q&A