

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

- 
- A vertical timeline with a dashed line and colored circular markers for each year. The years are listed on the left, and the corresponding events are listed on the right. The text is color-coded to match the markers: grey for 1990, blue for 2003, yellow for 2015, green for 2018, orange for 2020, and teal for 2021.
- 1990 ● Hormonal IUD first approved in Finland (Mirena®)
  - 2003 ● 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
  - 2015 ● 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**
  - 2015 ● 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
  - 2021 ● **M360 announces Avibela price subsidy for global procurement agencies through 2024**

Hormonal IUD pilot studies in LMICs

# History of Impact RH360 and Avibela

Medicines<sup>®</sup>  
**360** ♀

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



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

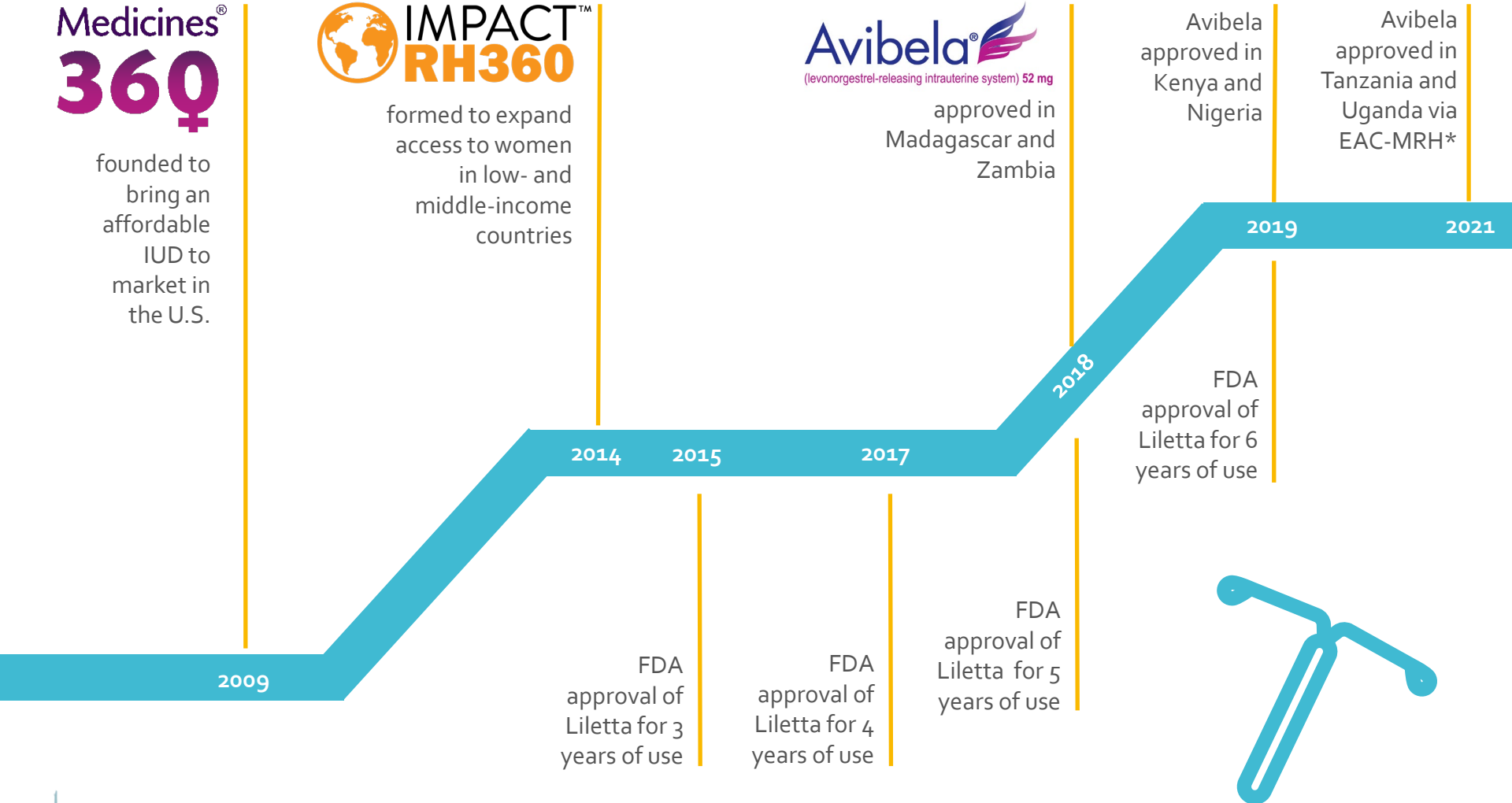


(levonorgestrel-releasing intrauterine system) 52 mg

approved in Madagascar and Zambia

Avibela approved in Kenya and Nigeria

Avibela approved in Tanzania and Uganda via EAC-MRH\*



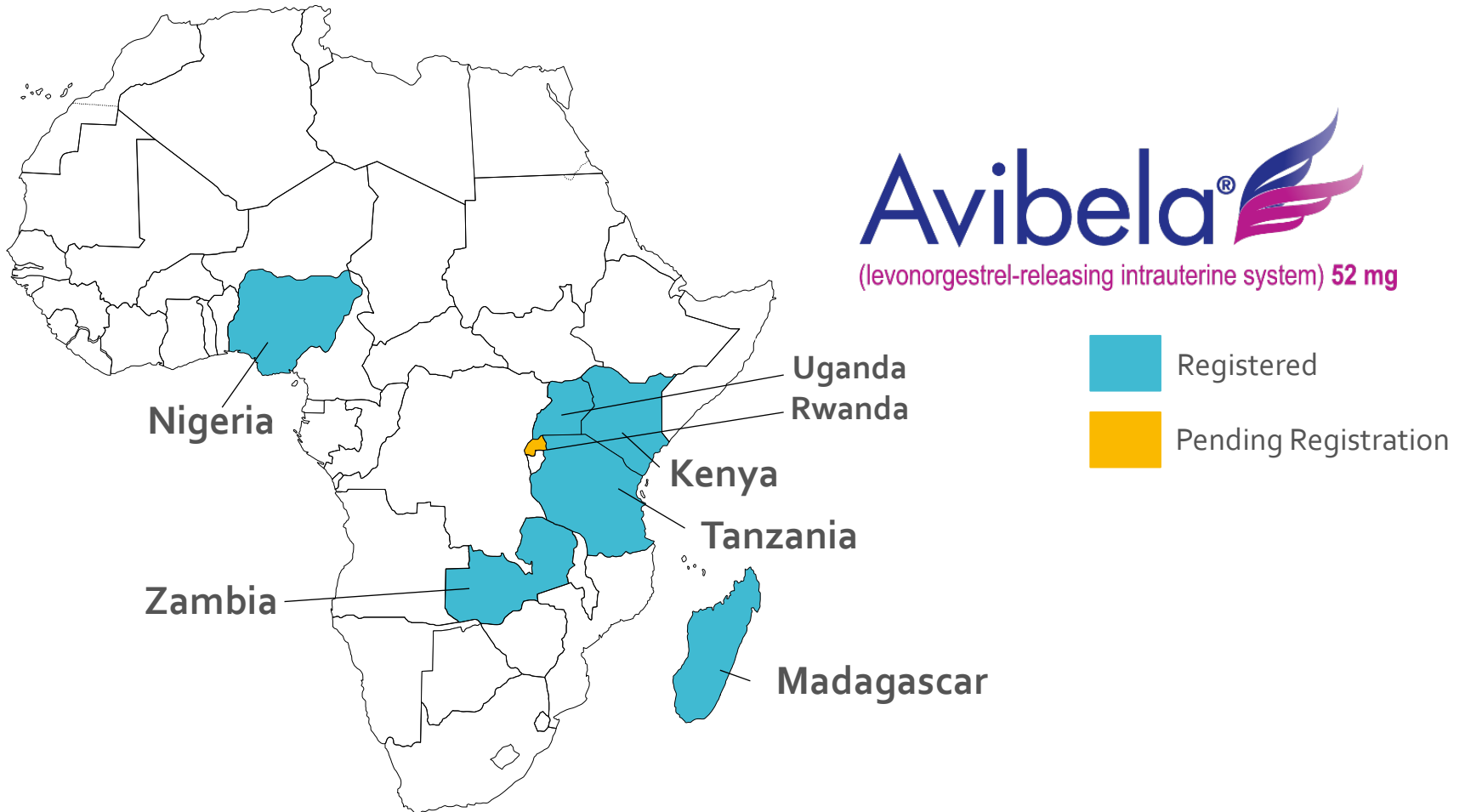
FDA approval of Liletta for 3 years of use

FDA approval of Liletta for 4 years of use

FDA approval of Liletta for 5 years of use

FDA approval of Liletta for 6 years of use

# Select Current and Pending Avibela Registrations



# 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



4001177

Sur prescription uniquement

# Avibela™

(système intra-utérin à libération de lévonorgestrel) 52 mg

1 Unité stérile | Utilisation par voie intra-utérine

**Veuillez lire les instructions relatives à l'insertion.**

**IMPORTANT : à insérer dans l'utérus par un professionnel de santé formé en suivant scrupuleusement les instructions d'insertion.**

Se reporter à la notice pour connaître les informations relatives au dosage.

Conserver à une température ne dépassant pas 30 °C.  
Conserver l'étui dans l'emballage externe jusqu'au moment de son utilisation pour le protéger de la lumière.

Non fabriqué à base de latex de caoutchouc naturel.

AVIBELA ne présente aucun danger pour l'examen par IRM.

**Sterile sauf si l'emballage est endommagé ou ouvert.**

Fabriqué par :  
Odyssea Pharma, Belgique,  
une filiale d'Allergan USA, Inc.

Distribué et commercialisé par :  
PSI/Madagascar  
Immeuble-FIARO  
Rue Jules RANAIVO  
ESCALIER-D, 2eme Etage  
BP 7748  
Antananarivo 101  
Téléphone : +261-20-22-629-84

WCG

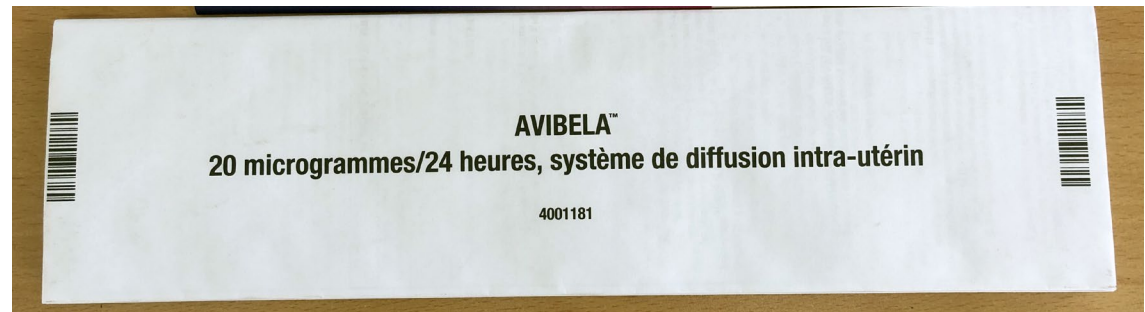
Ne pas insérer AVIBELA après la date de péremption imprimée sur cette étiquette.

Lot 17008-01  
Exp. 06/2021

Country specific information

# Non-Harmonized Labeling: Madagascar

## Summary of Product Characteristics and Prescribing Information



Prise de poids		Echographie ovarienne anormale			
Affections musculo-squelettiques et des tissus conjonctifs					
Affections du système nerveux		Céphalée			
Affections psychiatriques			Depression		
Affections des organes de reproduction et du sein	Saignements utérins/vaginaux comprenant micro-rapies, oligoménorrhée, aménorrhée, prolongation du cycle menstruel	Kyste de l'ovaire Dysménorrhée Sensibilité mammaire	Panarthrite, douleur pelvienne, salpingo-ophorite, polyarthrose		

Ces cas de septicémie (notamment une septicémie à streptocoques du groupe A) ont été signalés après l'insertion d'autres SIU hormonaux (voir la rubrique 4.4). Les réactions indésirables suivantes ont été signalées en lien avec l'insertion ou le retrait d'AVIBELA : douleur, saignements, réaction vasovagale liée à l'insertion avec vertiges ou syncope (voir la rubrique 4.4). La procédure peut aussi provoquer une crise d'épilepsie chez les patientes épileptiques. Le partenaire peut sentir les fils de retrait pendant les rapports sexuels.

**Déclaration des effets indésirables suspectés**  
La déclaration des effets indésirables suspectés après autorisation du médicament est importante. Elle permet une surveillance continue du rapport bénéfice/risque du médicament.

En cas de survenue ou de suspicion d'effets indésirables, merci de contacter dans les 24 heures :

- Le Supérieur Médical PSI ou le Coordonnateur Régional PSI de votre localité ou PSI (Tél. : 020 22 62984), et/ou
- Le Centre National de Pharmacovigilance de Madagascar - CNPV (Tél. : 20 22 365 22 poste 301)

### 7. TITULAIRE DE L'AUTORISATION DE MISE SUR LE MARCHÉ

PSI/Madagascar  
Immeuble- FIARO  
Rue Jules RANAIVO  
ESCALIER-D, 2ème Etage  
BP 7748  
Antananarivo 101  
Téléphone : + 261-20-22-629-84

### 8. NUMÉRO(S) D'AUTORISATION DE MISE SUR LE MARCHÉ

32.1.2.046

### 9. DATE DE PREMIÈRE AUTORISATION/DE RENOUELEMENT DE L'AUTORISATION

19/03/2018

### 10. DATE DE MISE À JOUR DU TEXTE

04/2018

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Country specific information

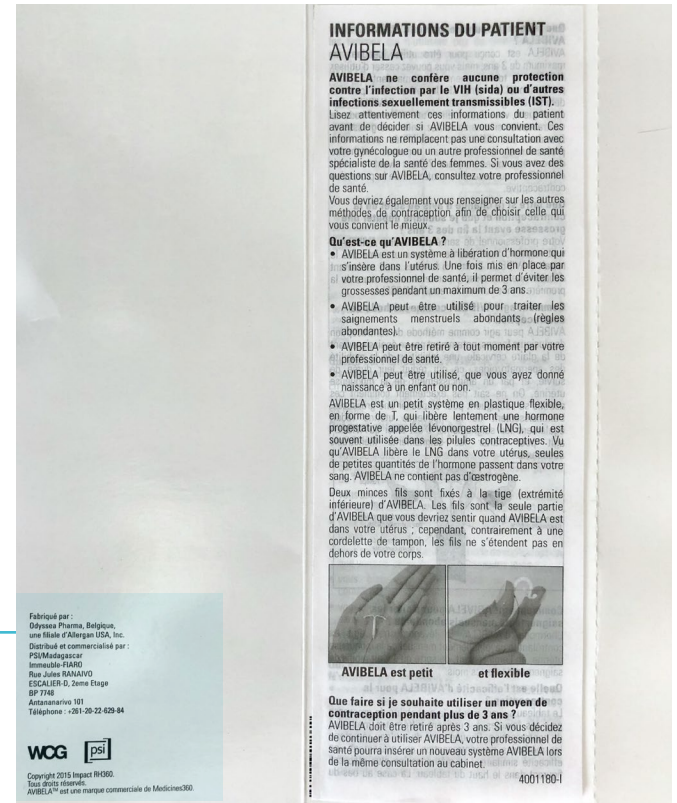
Country specific information

# Non-Harmonized Labeling: Madagascar

## Patient Information Leaflet

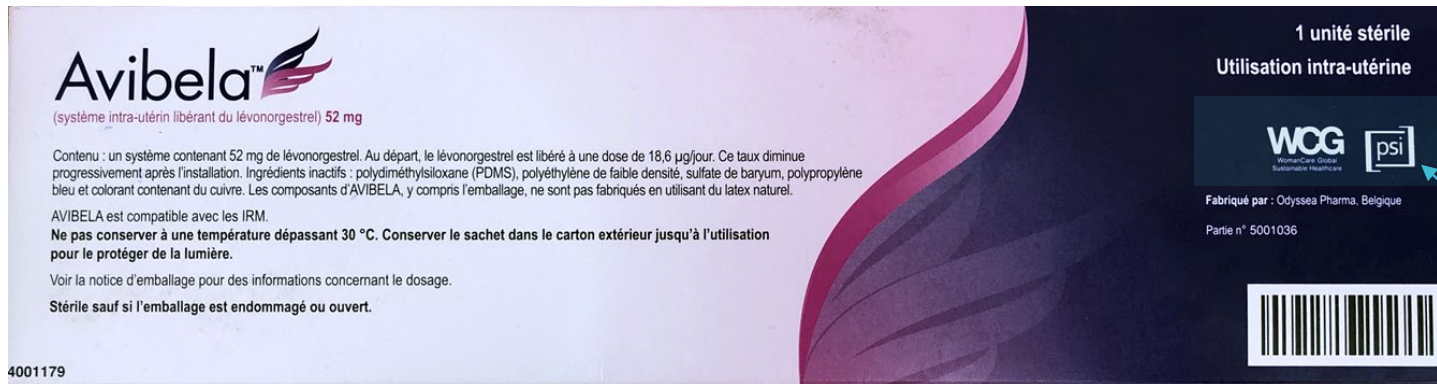


Country specific information



# Non-Harmonized Labeling: Madagascar

## Unit Carton



Country specific information



# Project Activities

Desk Review

Stakeholder Interviews

Labeling Development

# Key Takeaways

- 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

Component	Country-Specific Variable Information Required	Languages Required in 21 Countries Assessed
<b>Pouch Label</b>	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”	<ul style="list-style-type: none"> <li>• Afrikaans<sup>1</sup> (South Africa)</li> <li>• Bahasa (Malaysia)</li> <li>• English – 13 countries</li> <li>• French – 5 countries</li> <li>• Vietnamese (Vietnam)</li> </ul>
<b>Summary of Product Characteristics</b>	MAH name and address, contact info for AE reporting, registration number, scheduling status, date of first authorization & renewal. Note: format requirements also vary slightly	<ul style="list-style-type: none"> <li>• Afrikaans<sup>1</sup> (South Africa)</li> <li>• English – 14 countries</li> <li>• French – 5 countries</li> <li>• Vietnamese (Vietnam)</li> </ul>
<b>Patient Information Leaflet</b>	Local registration number, scheduling status. Note: required format also varies slightly	<ul style="list-style-type: none"> <li>• Afrikaans<sup>1</sup> (South Africa)</li> <li>• Bahasa (Malaysia)</li> <li>• English – 12 countries</li> <li>• French – 5 countries</li> <li>• Sinhala, Tamil (Sri Lanka)</li> <li>• Vietnamese (Vietnam)</li> </ul>
<b>Unit Carton</b>	MAH name & address, and local registration number	<ul style="list-style-type: none"> <li>• Afrikaans<sup>1</sup> (South Africa)</li> <li>• English – 14 countries</li> <li>• French – 5 countries</li> <li>• Vietnamese (Vietnam)</li> </ul>

# Interview Findings

**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

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

Current State

## 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

Kindaruma Road, Off Ngong Road

Kilimani, Nairobi

Phone: 0800 720 005 / 254 (0) 57 252 3 218

Email: [info@mariestopes.or.ke](mailto:info@mariestopes.or.ke)

#### The Pharmacy and Poison Board

Lenana Road

Nairobi

Phone: (020) 2716905/6 ext 114

Email: [pv@pharmacyboardkenya.org](mailto:pv@pharmacyboardkenya.org)

### Madagascar

#### PSI Madagascar

Immeuble ARBORETUM

Ex village des jeux ANKORONDRANO

ANTANANARIVO 101

Phone: + 261-20-22-629-84

#### Le Centre National de Pharmacovigilance de Madagascar - CNPV

Phone: 20 22 365 22 ext. 301

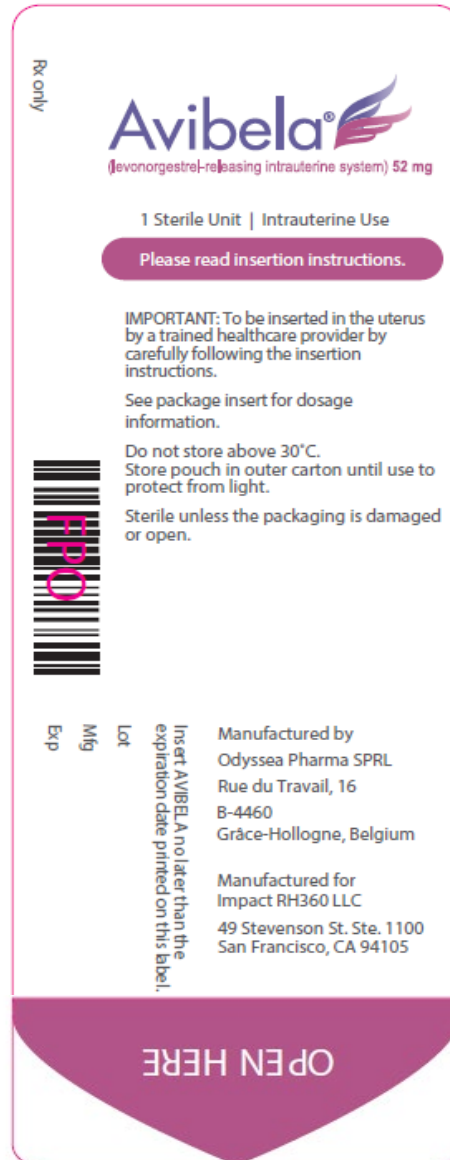
# Harmonized Labeling

*Pharmacovigilance Reporting Information*



# 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

Copyright 2021 Impact RH360 LLC  
All rights reserved.  
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](http://www.avibelapv.com).



*Removed local PV contact info and added global URL and QR code*

# Harmonized English

## Unit Carton



Marketing authorization number(s):  
Kenya: H2019/CTD5856/1070ER  
Zambia: 125/010  
Nigeria: NAFDAC REG. NO. 03-7235  
Tanzania: TAN 21 HM 0241  
Rwanda: TBD  
Uganda: NDA/MAL/HDP/9791

*Added all current product registration numbers (instead of listing only a few on pouch label)*

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

*Removed local distributor information*

# Next Steps

Post-approval  
variations

New filings

# Project Team



**Andree Sosler, MBA**

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Impact RH360



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Impact RH360



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**Mbavhalelo Jade Tshikosi, MS**

Global Regulatory Affairs  
Consultant



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Sr. Epidemiologist, Product  
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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

