WEBINAR

Harmonized Labeling for the Hormonal IUD in Low- and Middle-Income Countries

March 22, 2022, 7am PT / 10am ET

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IMPACT™ RH360

fhi360 THE SCIENCE OF IMPROVING LIVES

WCG EMPOWER EDUCATE ENABLE

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

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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

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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

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The Hormonal IUD in LMICs

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History of Impact RH360 and Avibela

2009

Medicines 360 founded to bring an affordable IUD to market in the U.S.

2014

IMPACT RH360 formed to expand access to women in low- and middle-income countries

2015

FDA approval of Liletta for 3 years of use

2017

FDA approval of Liletta for 4 years of use

2018

Avibela (levonorgestrel-releasing intrauterine system) 52 mg approved in Madagascar and Zambia

FDA approval of Liletta for 5 years of use

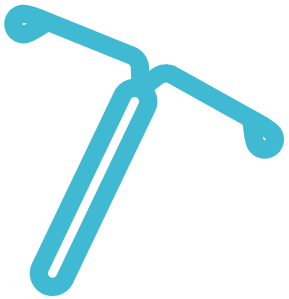
2019

Avibela approved in Kenya and Nigeria

FDA approval of Liletta for 6 years of use

2021

Avibela approved in Tanzania and Uganda via EAC-MRH*



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*East African Community Medicines Regulatory Harmonization program

Select Current and Pending Avibela Registrations

Avibela®
(levonorgestrel-releasing intrauterine system) **52 mg**

Registered

Pending Registration

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The Case for Harmonized Labeling

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Key Challenges to Harmonization

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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

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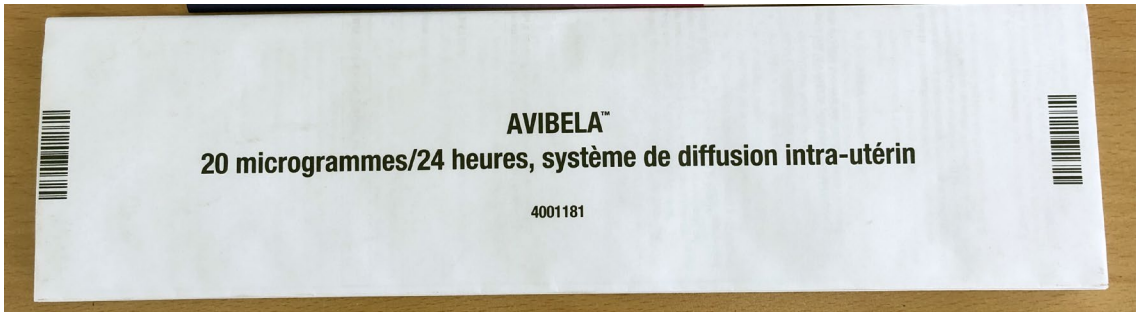
Non-Harmonized Labeling: Madagascar

Pouch Label

Country specific information

Non-Harmonized Labeling: Madagascar

Summary of Product Characteristics and Prescribing Information



...ne...sations		Prise de poids Échographie ovarienne anormale			
Affections musculaires, squelettiques et des tissus conjonctifs					
Affections du système nerveux		Céphalée			
Affections psychiatriques			Dépression		
Affections des organes de reproduction et du sein	Saignements utérins/ vaginaux comprenant micror ragies, oligoménorrhée, aménorrhée, prolongation du cycle	Kystes de l'ovaire Dysménorrhée Sensibilité mammaire Saignements menstruels abondants	Paraménite, douleur pelvienne, salpingo-ovarite, polyménorrhée		

Des 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 Superviseur 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 Étage
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 RENOUVELLEMENT DE L'AUTORISATION

19/03/2018

10. DATE DE MISE À JOUR DU TEXTE

04/2018

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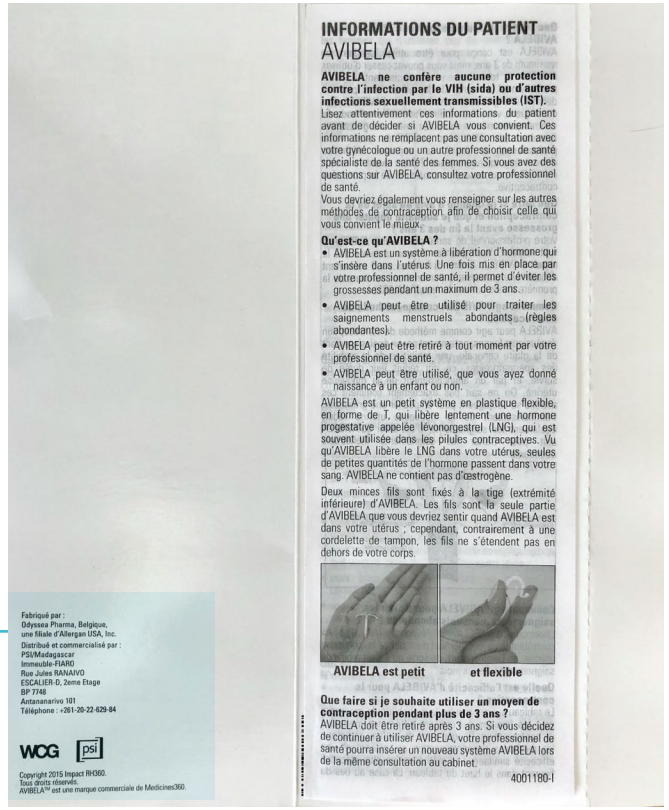
Avibela® est une marque de Medicines360.

Country specific information

Country specific information

Non-Harmonized Labeling: Madagascar

Patient Information Leaflet



Country specific information

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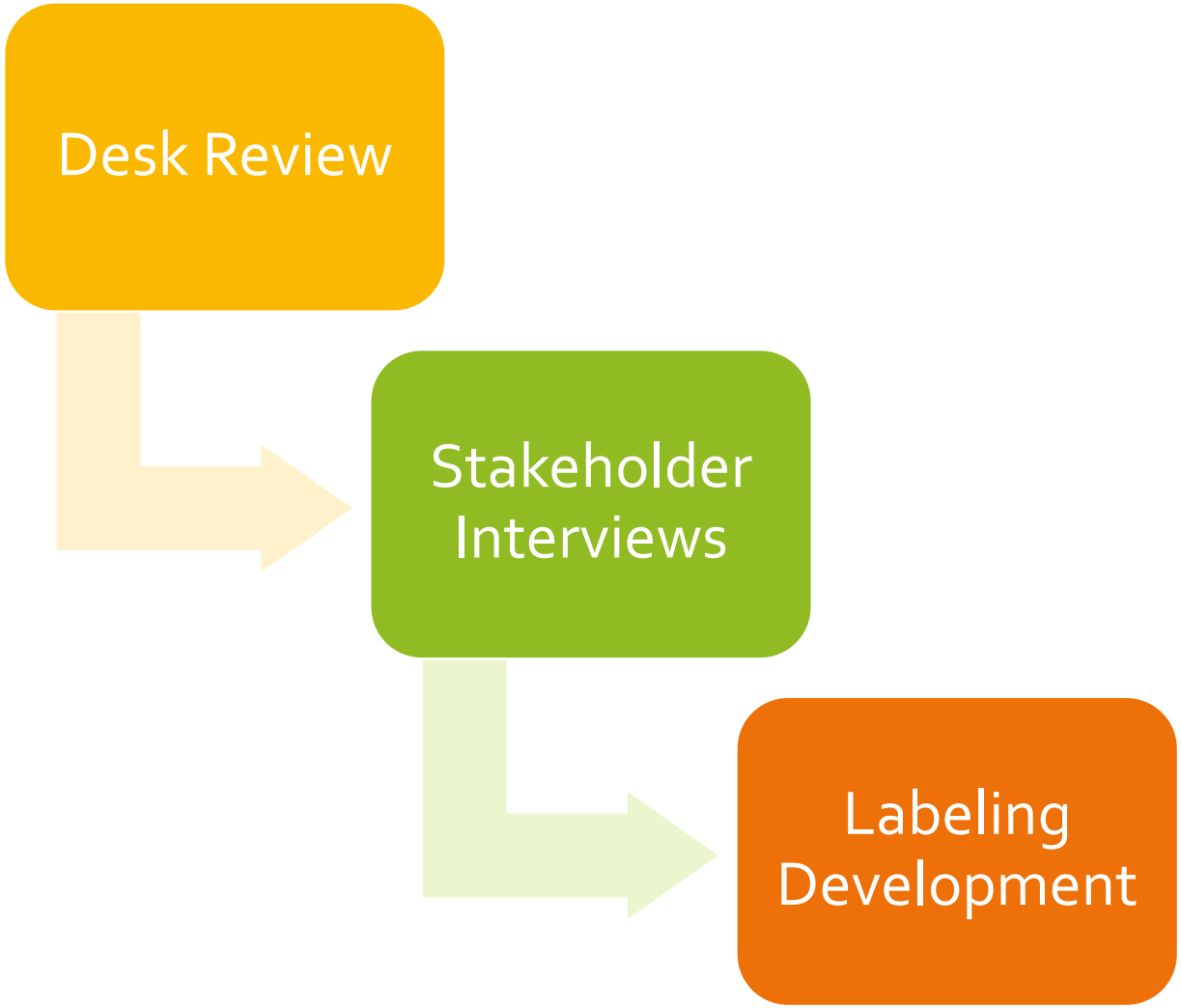
Non-Harmonized Labeling: Madagascar

Unit Carton

Country specific information

Project Activities



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
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"	• Afrikaans[1] (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	• Afrikaans[1] (South Africa) • English – 14 countries • French – 5 countries • Vietnamese (Vietnam)
Patient Information Leaflet	Local registration number, scheduling status. Note: required format also varies slightly	• Afrikaans[1] (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	• Afrikaans[1] (South Africa) • English – 14 countries • French – 5 countries • Vietnamese (Vietnam)

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1 Or any of South Africa's other 12 local languages

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

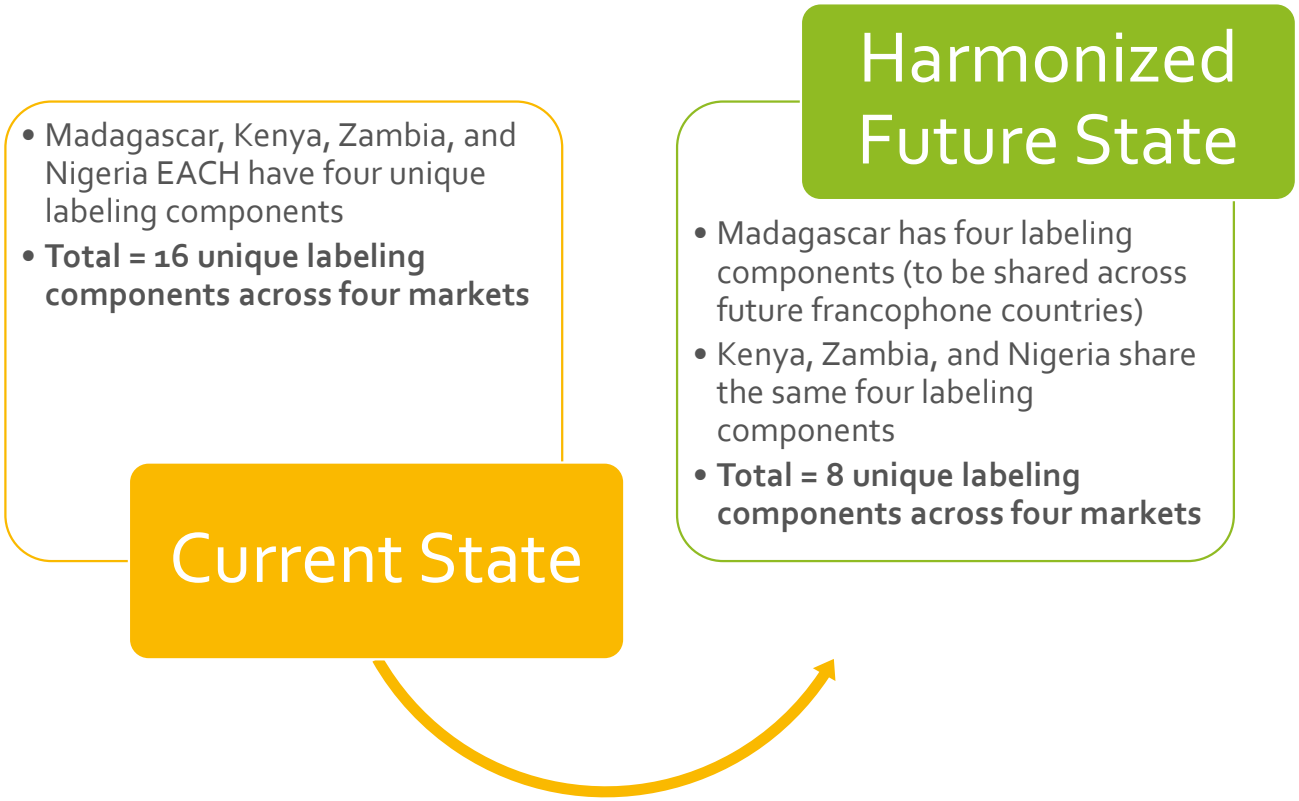
- Does not require the manufacturer to validate new labeling sizes
- Allows Avibela to achieve some level of harmonization in the relative short-term

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



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

The Pharmacy and Poison Board

Lenana Road

Nairobi

Phone: (020) 2716905/6 ext 114

Email: 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

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Harmonized Labeling

Pharmacovigilance Reporting Information

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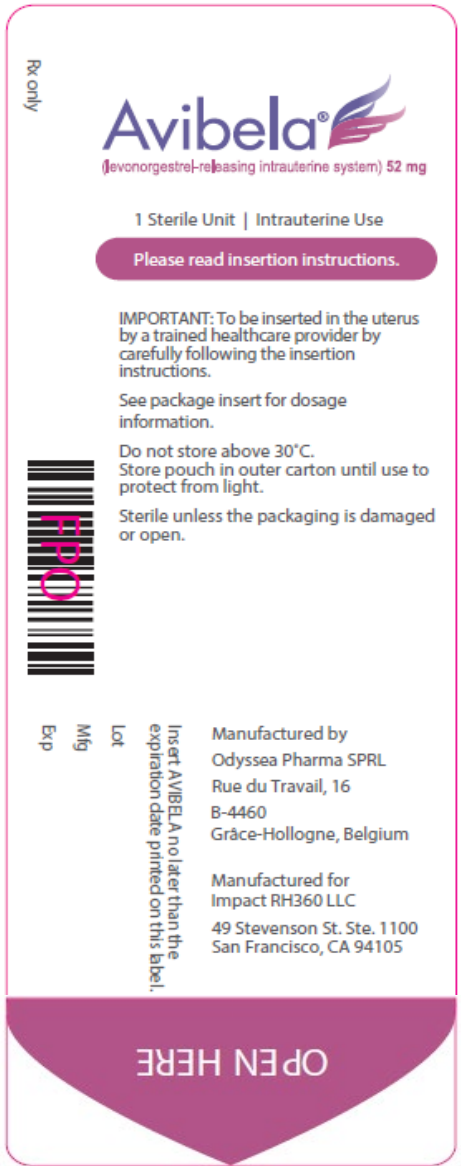
Harmonized English

Pouch Label and Directional Sticker



- *Removed distributor information*
- *Removed product registration numbers*

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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.

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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

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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

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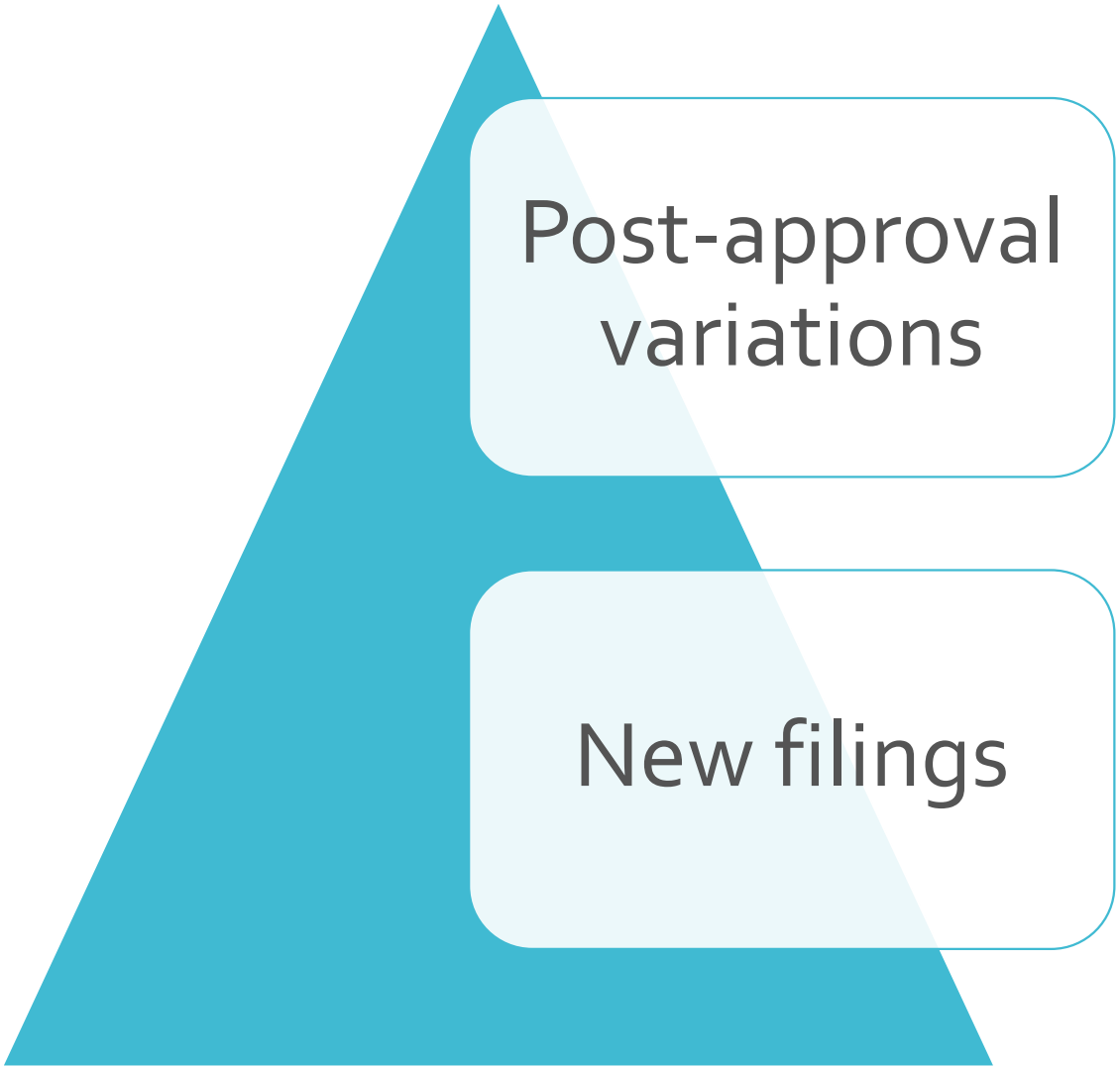
Next Steps



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FHI 360

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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

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Q&A