



# Parallel Imports - Common errors and omissions

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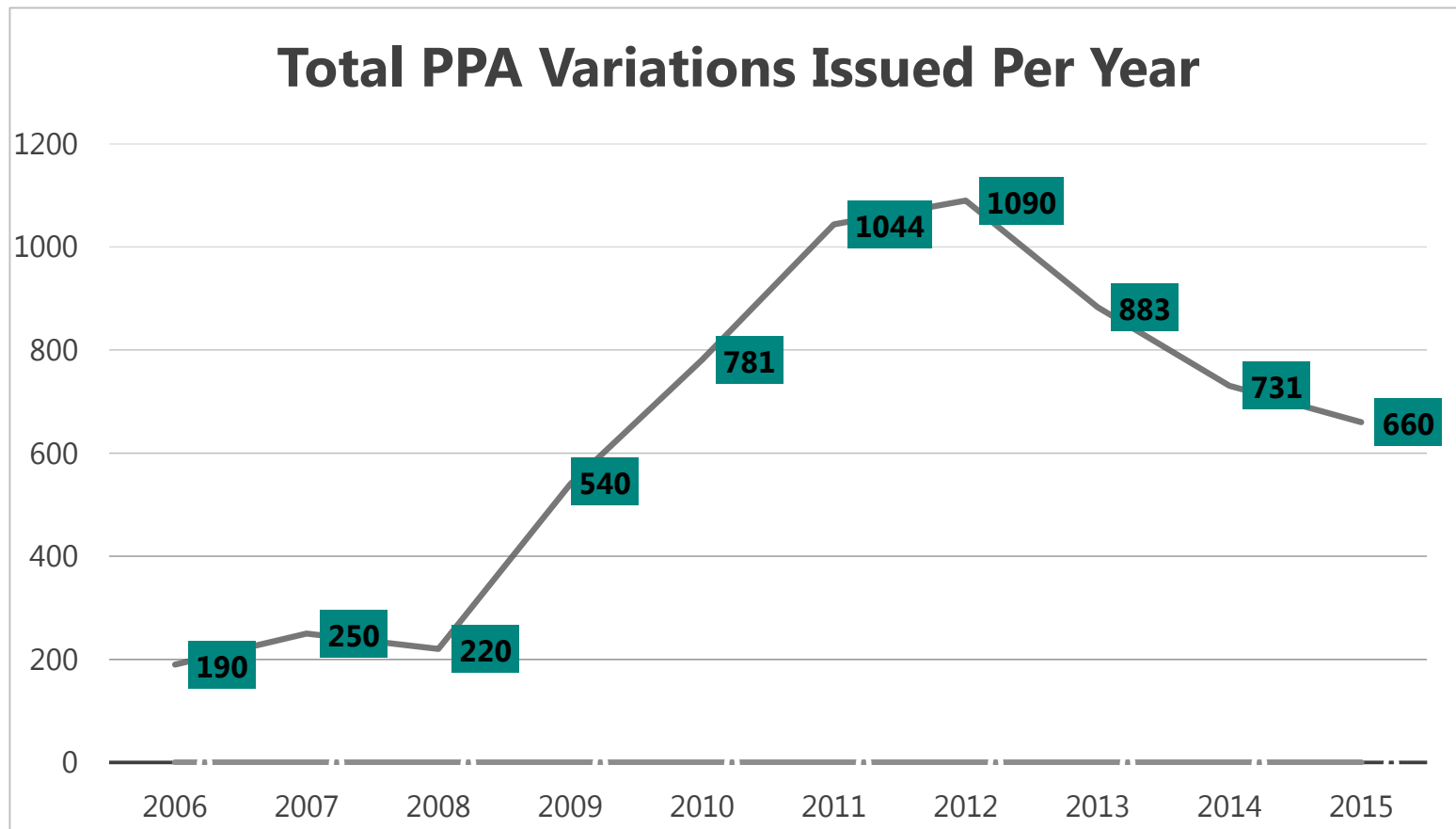
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**HPRA PPA Webinar**

HPRA Offices, 10/03/14



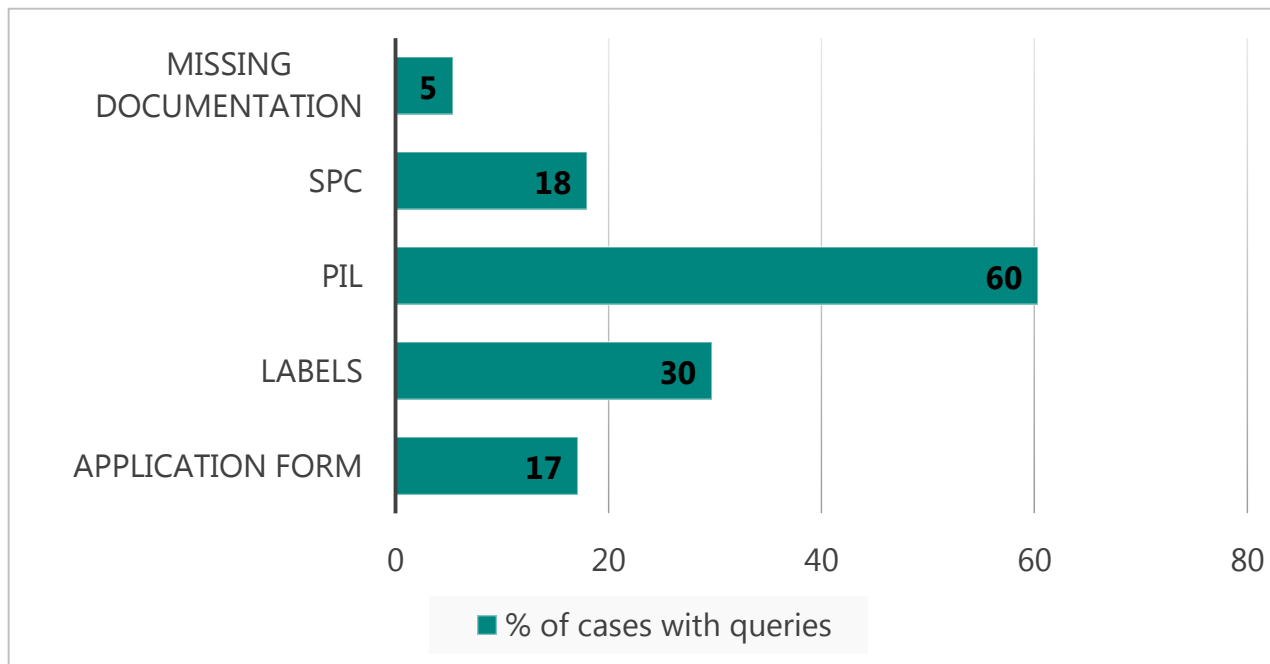
## Trends in PPA submissions





## Statistics

- Sample of 200 variations from the last 6 months
- 55.5% of PPA cases submitted since July 2015 required queries.





## Statistics

	2010	2016
Total cases requiring query	60%	55.5%
Cases requiring > one round of queries	15%	17.5%

# Introduction

## Aim

- To reduce the rounds of correspondence required between the HPRA and PPA applicants by eliminating the common errors and omissions in PPA applications.

## Background

- Many PPA application types generally require one or more rounds of correspondence to complete the assessment.
  - Most queries relate to
    - Changes to SmPC
    - Changes to label/leaflet
    - Requesting a sample
    - Requesting additional supporting documentation

# Overview

- Electronic Submissions
- Application Form
- Preparing product information
  - SmPC
  - Label
  - Leaflet
  - Braille
- Summary

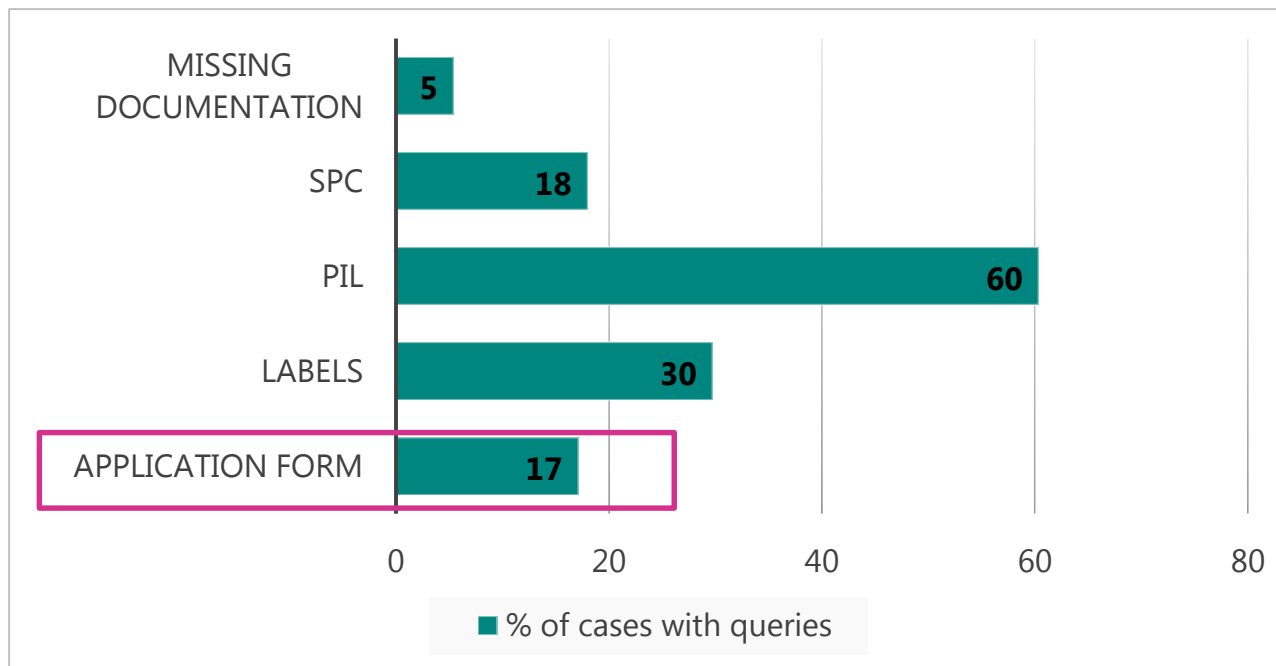
# Electronic Submissions

- Electronic submission is the HPRA's format for receiving applications.
- Samples are only required when requested. However, when requested, full samples must be provided i.e. the entire product presentation.
- When providing scans, supply in full and in clearly legible form.
- New Parallel Import Applications (PPAs), Additional Source Country Applications, PPA Variations, PPA Renewals are accepted by the HPRA as simple Word/PDF submissions without requiring additional paper copies.

(No duplication is necessary; one copy of each document in electronic format (Word/PDF) is sufficient.)

- See HPRA guide to electronic submissions for further info
- When responding to queries, please respond to all HPRA staff listed on the original email.

# Application Form





# Application Form

- The most recent application form templates should always be used (available at [www.hpra.ie](http://www.hpra.ie) under publications).
- Guidance on completing the forms is set out in Annex 2 of the Guide to Parallel Imports. It is very important to use this to ensure applications are complete.
  - All sections of the form should be completed in full.
  - **For new sources**, the comparative product details should be completed in full as per the guide;
    - Irish marketed product details from the Irish SmPC.
    - Source country product details from the source country leaflet/packaging.
  - For variations, a brief background explanation for the change and present/proposed details should be completed in full in every instance. **This is often omitted.**

# Application Form

- A fully-complete application form facilitates quicker assessment and less rounds of correspondence.
- **EXAMPLE:**

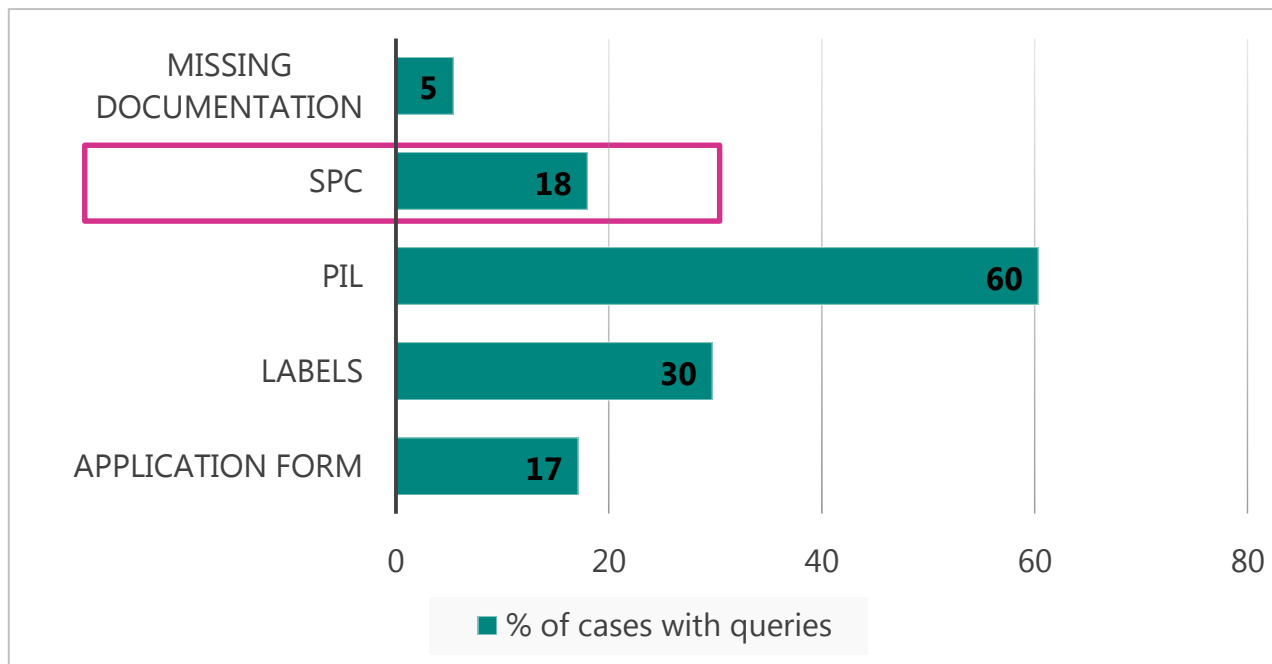
Full information on source country product composition is not provided, requiring correspondence.

The decision on TEq depends on the composition and other details. This is much easier to do with a well laid out comparative table. Example....

# Application Form

Comparative Product Details	Ireland	Member State or EEA Country
Marketing Authorisation Number	PA 1111/222/33	1234567
Name and address of Marketing Authorisation Holder	Name: Dublin Pharma Address: Goldenlane, Silver Street Business Park Dublin 20	Name: Dublin Pharma Address: Silverlane, Athens Industrial Estate Athens Greece
Name of product strength and pharmaceutical form	Paracetamol 500 mg Capsules	Paracetamol 500 mg Kapsuly
Name of active substance	Paracetamol	Paracetamol
Line list of excipients	Lactose Methylcellulose Povidone K30 Gelatin	Lactose Methylcellulose Povidone Gelatin
Storage conditions on label of product as marketed	Do not store above 25°C	Do not store above 25°C
Container type(s) and pack size(s)	PVC/Aluminium blister packs packed in a cardboard carton to contain 28 capsules	PVC/Aluminium blister packs packed in a cardboard carton to contain 28 capsules
Name and address of manufacturer, as declared in the package leaflet	Dublin Pharma, Earlsfort Terrace, Dublin 2, Ireland	Dublin Pharma, Earlsfort Terrace, Dublin 2, Ireland

## Preparing product information: Summary of Product Characteristics



# Summary of Product Characteristics

- The pharmaceutical information of the SmPC must be based on both the reference product SmPC and the source country leaflet/label – SmPC sections 2, 3, 6
- The clinical information of the SmPC must cross reference the Irish reference SmPC – SmPC sections 4 and 5
- See **HPRA Guide to Parallel Imports** and the [annotated QRD template](#) for SmPC and other product information layout/contents
- Always refer to the HPRAs website for the most recent SmPC of the Irish reference product:

<http://www.hpra.ie/>

Click the icon 'View & Search Product Listings- Human'

- The information on the website is produced from HPRAs databases and is normally updated every 7 days.

**It should be the primary reference point.**

# Summary of Product Characteristics

## Section 1: Name of the medicinal product

- The proposed product name should be as per the Irish reference product:

“Brand Name, Strength, Pharmaceutical Form”

- This product name should appear prominently on the immediate and outer packaging and at the start of the package leaflet **as a cohesive unit** followed by the active substance name.

*Invented Name, Strength, Pharmaceutical Form*

*Active substance*

# Summary of Product Characteristics

## Section 2: Qualitative and quantitative composition

- Active substance content should be clearly stated and a reference to any salt/hydrate forms included if appropriate
- Excipients with a recognised action or effect must be stated in this section.

(see [Guide on excipients in the label and package leaflet of medicinal products for human use CPMP/463/00](#) for a full list)

- Quantities of excipients should only be stated if they can be confirmed from the source country product info.
  - If not explicitly stated in the source country product info, leave out the quantity
  - *Example*  
'Contains 45 mg lactose monohydrate'

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  - *Example*  
'Contains ~~45 mg~~ lactose monohydrate'



# Summary of Product Characteristics

## Section 3: Pharmaceutical form

- The visual description should be a description of the source country product- not copied directly from Irish reference product SmPC.
  - e.g. Different markings, shape, scorelines.
- Inclusion of a scoreline statement must be supported by the source country product information.

*Example: "The tablet can be divided into equal doses"*

- A product parallel imported from more than one Member State may differ in appearance. Differences should be clearly stated in this section.

# Summary of Product Characteristics

## Section 4: Clinical Particulars **SINCE SEPTEMBER 2014**

- As per *<include PA number of Irish product>*
- Where an excipient with a recognised action or effect is declared on the label, the relevant warning must be included in the SmPC, in section 4 as appropriate. This can arise where the composition differs between the source country product and the Irish reference product.

(see [Guide on excipients in the label and package leaflet of medicinal products for human use CPMP/463/00](#))

## Section 5: PHARMACOLOGICAL PROPERTIES

- As per *<include PA number of Irish product>*

# Summary of Product Characteristics

## Section 6.1: List of excipients

- The list of excipients should be drawn up from the source country product info. and not copied directly from Irish reference product SmPC.
- If there are differences in excipients between separate source countries, separate lists should be given, related to the Member States from which the product is to be parallel-imported.

# Summary of Product Characteristics

## Section 6.3: Shelf life

- The standard statement for PPAs should **always** be used:

*“The shelf life expiry date of this product is the date shown on the container and outer carton of the product as marketed in the country of origin.”*

- If an in-use shelf life is referred to in the Irish reference product or the source country product information then those details should also be stated here.
- **If the information differs always favour the more conservative in-use shelf life.**
- *Example*  
“Discard 4 weeks after first opening”

# Summary of Product Characteristics

## Section 6.4: Special precautions for storage

- The storage statements on the label of the Irish-market product may be different from those on the container of the source country product.
- **If the information differs, always favour the more conservative storage statement.**

### *Example 1*

- Irish product states:  
"Do not store above 25°C"
- Source country product states:  
"Do not store above 30°C"

# Summary of Product Characteristics

## Section 6.4 Special precautions for storage

### *Example II*

- PA product states:

“Do not store above 25°C”

- Source country product states:

“No almacenar por encima de 25°C. Conservar en el embalaje original para protegerlo de la luz y la humedad.”

PPA product should state:

“Do not store above 25°C. Store in the original package in order to protect from light and moisture.”

# Summary of Product Characteristics

## Section 6.5 Nature and contents of container

- The composition of the packaging should only be stated if it can be confirmed from the source country product info.
- Delete any references to composition that cannot be confirmed.
- *Example*  
“PVC/PPA/Aluminium blister strips. 7 tablets per strip.  
Pack size 28 tablets.”

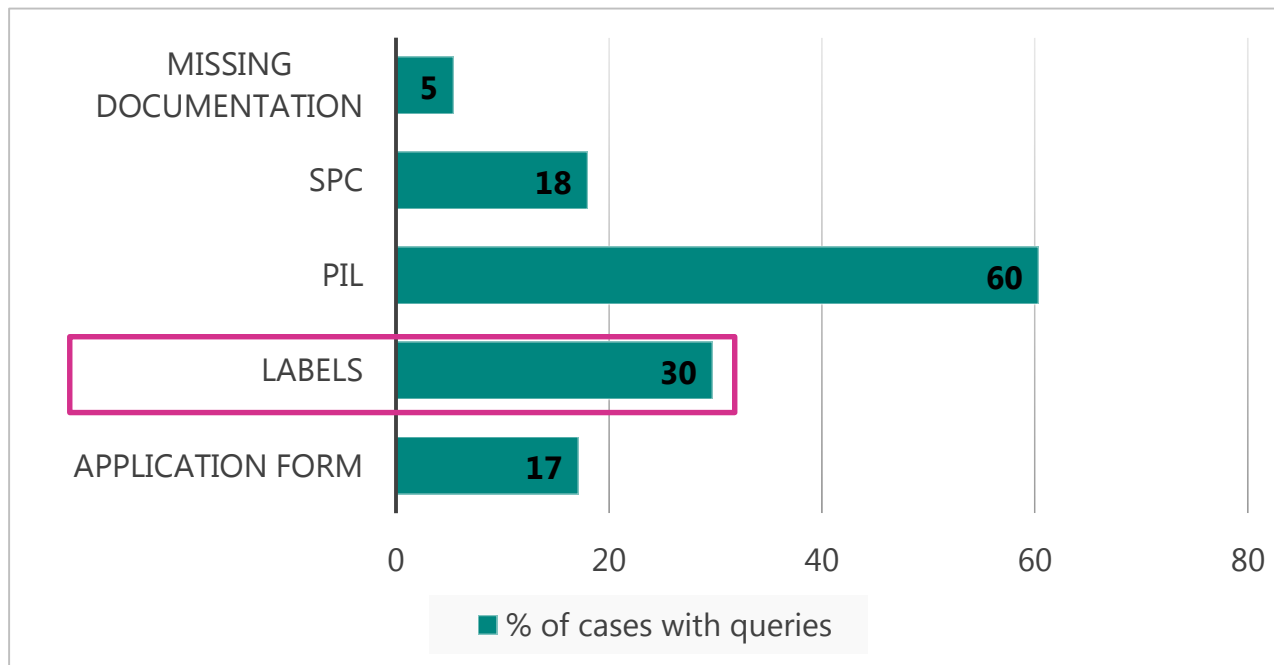
# Summary of Product Characteristics

## Section 6.5 Nature and contents of container

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- Delete any references to composition that cannot be confirmed.
- *Example*  
“~~PVC/PPA/Aluminium~~ blister strips. 7 tablets per strip.  
Pack size 28 tablets.”



## Preparing product information: Labels



# Labels

- Detailed guidance on the information required to be stated on PPA labels is outlined in the **HPRA Guide to Parallel Imports-Human Medicines**.
- Full colour mock-ups of the immediate and outer labels are required to accompany each application for a New PPA, an Additional Source country, or Renewal.
- For PPA variations, a mock-up of the overlabel is required.
- Mock-ups of labels should be an accurate representation of how the product will appear on the market (i.e. all sides of the proposed packaging should be visible and all text, both existing and overlabelled, should be legible).

# Labels - common errors/omissions

- Not highlighting the proposed changes to the labels
- Product name not in line with SmPC Section 1
- Excipient not stated on the label as per SmPC Section 2
- Full pharmaceutical form as per SmPC Section 3 missing
- Excipient list not in line with SmPC Section 6.1 (for inhalers/parenterals/topical products)
- Storage conditions not in line with SmPC Section 6.4
- “Keep out of the sight and reach of children” not as per QRD template

# Labels - common errors/omissions

- Method and route of administration missing
- Directions for use missing
- Not all manufacturers stated
- Spelling, typos, version control
- Expiry date, batch number, repackaging code, PPA number missing (for new PPA applications, a PPA number can be requested prior to submission)

# Labels – other considerations

Specific warning text that appears on the reference product labels missing e.g.

- Warnings on Paracetamol-containing products.
- “Do not crush or chew”.
- “Do not use in eyes.” for Aciclovir cream.
- “WARNING: FOR USE BY MEN ONLY” for some Finasteride tablets.

# Labels – overlabelling issues

- Note: If some of the required label text is already on the source country product in English and will be visible to the patient, these items **do not** have to be repeated on the source country label.

## *Examples*

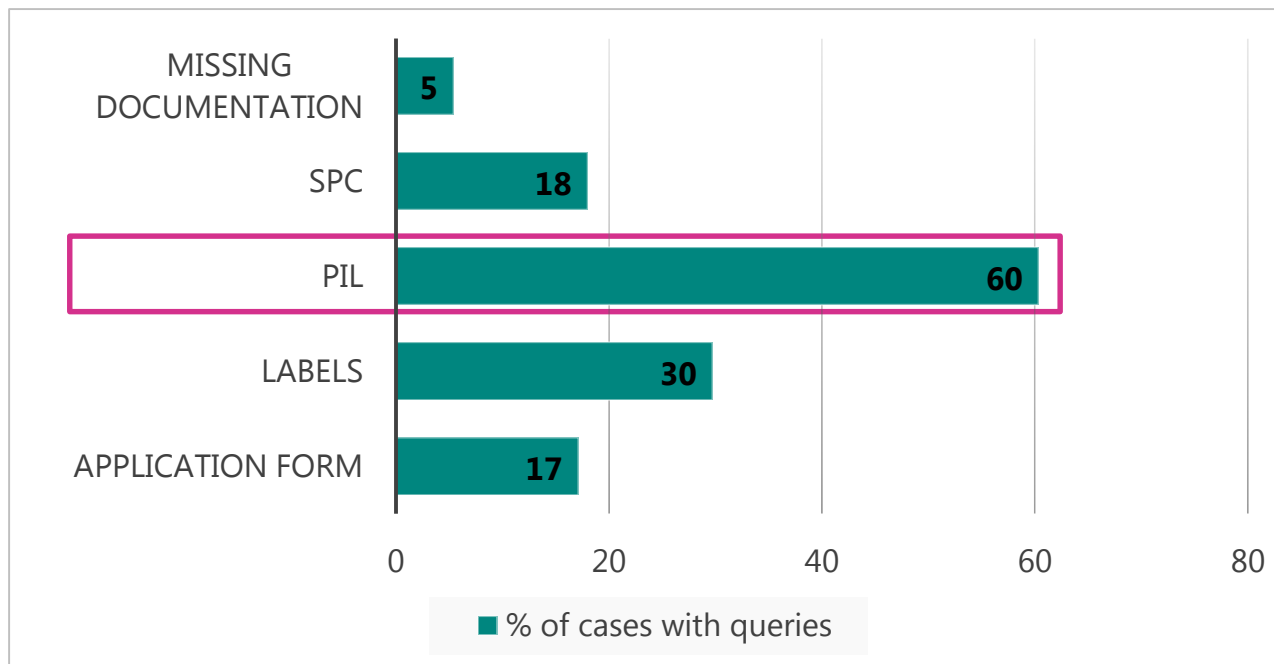
*Storage conditions, statement of content, excipient list.*

- The following abbreviations are reserved for reference to the original manufacturers batch number only and should not be used to denote internal batch numbers/repackaging codes;
  - BN
  - Lot
  - Batch

# Labels – overlabelling issues

- Where source country product packaging states conflicting information (e.g. *dosage or storage instructions*), this information should be obscured by the overlabel.
- To avoid confusion, where an source country product has a different name to that proposed in the PPA application, the existing name should be overlabelled with the proposed name in all instances on the outer packaging.
- This also applies to blister strips and other immediate packaging types.

## Preparing product information: Package Leaflet

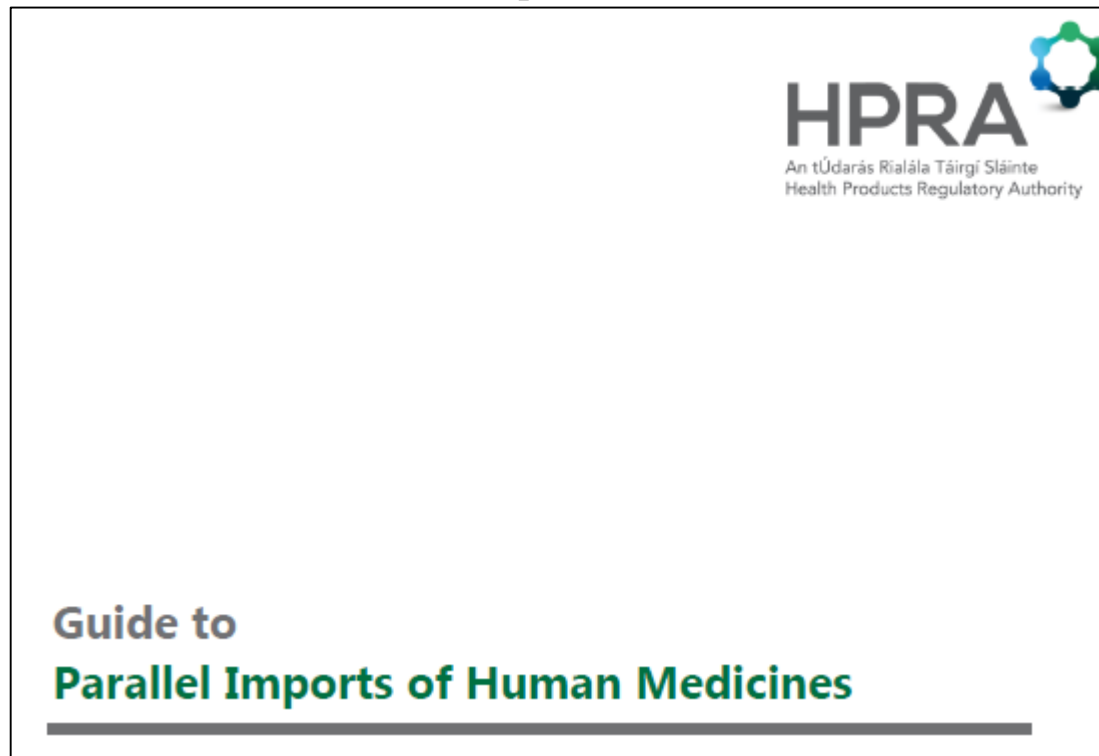




# Package Leaflet

- Detailed guidance on the information required to be stated in PPA package leaflets is outlined in the revised:

## HPRA Guide to Parallel Imports- Human Medicines



# Package Leaflet

- The pharmaceutical information of the PIL must be based on the PPA SmPC – PIL sections 5 and 6
- The clinical information of the PIL be identical to the Irish reference PIL – PIL sections 1, 2, 3, and 4.

# Package Leaflet- common errors/omissions

- Leaflet layout not in line with Irish reference product
- Section 1: Product name not in line with SmPC
- Section 1: Indications/directions for use in line with source country product info rather than Irish reference product
- Section 2: Excipient warnings not stated as per CPMP/463/00 and SmPC Section 4
- Section 5: Storage conditions not in line with SmPC Section 6.4

# Package Leaflet- common errors/omissions

- Section 5: Excipient list not in line with SmPC Section 6.1
- Section 6: Not all manufacturers stated
- Additional information for healthcare professionals omitted
- Spelling, typos, version control
- See [annotated QRD template](#) for recommendations for leaflet layout/contents
  
- Please note: Separate PILs (and labels) are not required for different repackagers – both can be listed on a single PIL
- Similarly, separate PILs are not required for different source countries if the pharmaceutical information is correctly listed

# Summary

- Five key areas to focus on:
  - **Clinical information** is in line with Irish reference product
  - **Pharmaceutical information** is correct and specific for each source country product
  - **Consistent content** in proposed SmPC, label & leaflet
  - Label/leaflet information should provide **the same level of detail** as the Irish reference product
  - **Version control**, spelling and typo checks NB!

# Summary

- Applicants should perform regular quality control (QC) checks on submissions to ensure compliance with current guidance.
- Correcting the common errors and omissions in PPA applications will greatly improve the efficiency of the assessment process and reduce the rounds of correspondence required. Saving resources for both PPA companies and the HPRA.

**Thank you!**



**Questions?**