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Solid Oral Immediate-Release Drug Product Landscape and Bioequivalence Recommendations

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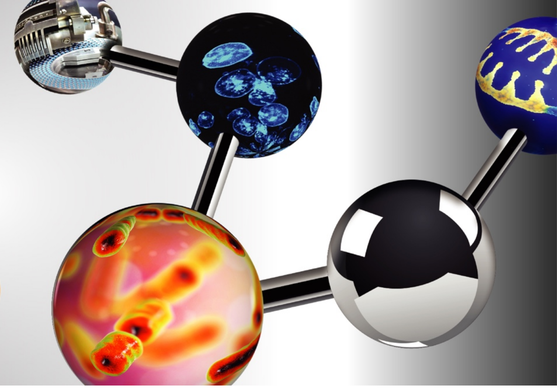


PURPOSE

- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) seeks to harmonize bioequivalence (BE) standards for generic drugs beginning with a guideline on bioequivalence for immediate-release (IR) oral solid dosage form drug products (ICH M13) (www.ich.org)
- To support this effort, we aim to obtain a comprehensive landscape of oral IR products approved by the U.S. Food and Drug Administration (FDA) and evaluate the current BE methods recommended by the U.S. FDA for these products

OBJECTIVE(S)

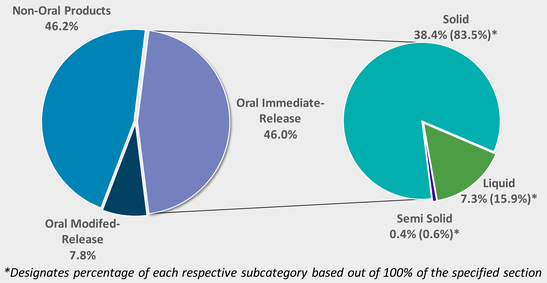
- Develop a full representation of the FDA's current approved oral IR drug product landscape
  - Categorize oral IR products into solid, liquid (solution/suspension), or semi-solid dosage forms
  - Characterize products by New Drug Application (NDA), availability of generics, and Product-Specific Guidances (PSGs)
- Investigate current BE study recommendations for all solid oral IR products
  - Delineate different BE approaches and fast/fed considerations

METHOD(S)

- We utilized databases including Drugs@FDA, Orange Book, and the PSG database to collect information about the U.S. FDA-approved drug products and BE recommendations
- The PSGs' Additional Comment section was reviewed to highlight special considerations for drug administration and any potential patient and/or industry impact

RESULT(S)

Complete Oral IR Landscape



**Designates percentage of each respective subcategory based out of 100% of the specified section*

RESULT(S)

IR Product Dosage Form Summary

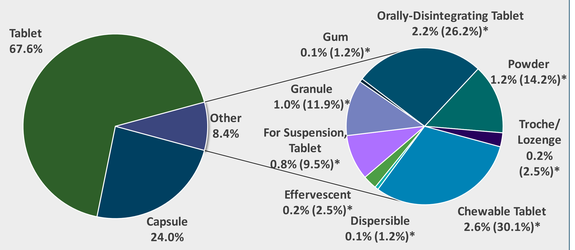
Solids	Liquids	Semi-Solids
• Capsule • Chewable Tablet/Bar • Dispersible Tablet • Effervescent Tablet • For Solution/Suspension Tablet • Granule • Gum • Orally Disintegrating Tablet (ODT) • Powder • Tablet • Troche/Lozenge	• Concentrate • Elixir • Emulsion • For Solution/Suspension • Solution • Suspension • Spray	• Film • Gel • Paste

PSGs' Additional Comment Section Summary

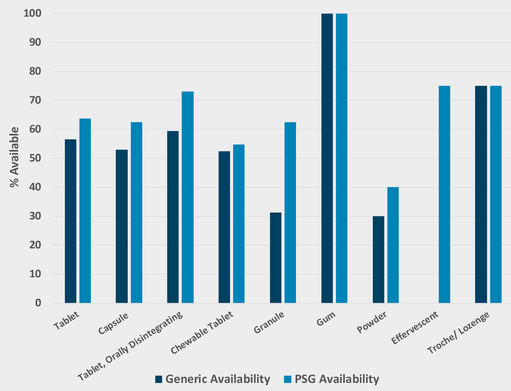
Dosage Form	Dosage Form Description	Special Administration Consideration in BE Studies
Orally-Disintegrating Tablet	• Solid oral dosage form containing medicinal substances that disintegrate rapidly, usually less than 30 seconds, when placed upon the tongue	• Per PSGs, patients advised to either take with or without water based on Reference Listed Drug (RLD) labeling • If labeling indicates with or without water options, PSG will indicate to take without water
Chewable Tablet	• Solid oral dosage form intended to be chewed and then swallowed; generally designed to be palatable and easily crushed • Potential to be swallowed whole, impacting bioavailability and the patients' therapeutic drug levels	• When RLD labeling states the tablet must be chewed before swallowing, the PSG will indicate the products should be chewed when administered • When RLD labeling give options of either chewing or swallowing whole, the PSG will indicate the product should be swallowed whole, with 240 milliliters of water
Effervescent Tablet	• Solid oral uncoated tablets containing acidic excipients and carbonates that react rapidly when placed in water to release carbon dioxide	• All effervescent products are added to liquids before drug consumption • Patient always consumes drug after dissolution of drug into a solution
Granule	• Solid oral dosage form containing particles which have been aggregated to form large granular material with diameter of approximately 2-4 mm	• Granules are generally required to be administered with soft food before consumption such as applesauce, pudding, yogurt, or mashed potatoes • Effervescent granules require mixing with liquids rather than food
Powder	• Solid oral dosage form containing dry mixtures of finely divided, crushed, or grinded, medicinal substances varying from 10 nm-1000 µm in size	• Oral powder generally requires combination with liquids before consumption • Some products require food specific combination due to poor solubility of API • Some products require neither food nor liquids during administration

Recommendations in PSGs are in general aligned with the FDA Draft Guidance, *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application* (Aug 2021).

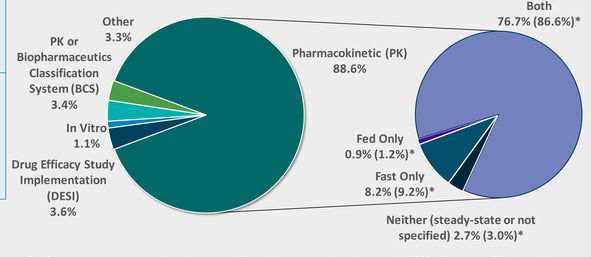
Solid Oral IR Landscape



Solid Oral IR Dosage Forms' PSG and Generic Availability



Solid Oral IR BE Recommendations



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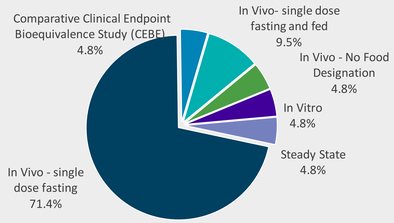
RESULT(S)

BE Recommendations for Sublingual and Buccal Products



CONCLUSION(S)

- This work provides a comprehensive landscape of all FDA-approved oral IR drug products.
  - Over 20 different oral IR dosage forms with approximately 2,000 unique active pharmaceutical ingredients (APIs)
  - Solid oral IR products, which is the focus of ICH M13 guideline under development, account for over 80% of oral IR products
  - For most solid oral IR products, both generic and PSG availability exceed 50%
- Majority of BE recommendations for the solid oral IR products are in vivo PK BE studies. Over 85% of in vivo PK BE studies recommend both a fasting and a fed BE study.
- Additional Comments section in PSG is related to drug administration or offers guidance on subject inclusion/exclusion criteria, safety precautions, and/or product characterizations.
- Additional work is needed to investigate whether some specialty solid oral IR dosage forms are candidates for potential waiver of fed BE studies, e.g., products presented as solids but intended to be administered as solution.

FUNDING AND REFERENCE(S)

Disclaimer: This poster reflects the views of the authors and should not be construed to represent FDA's views or policies.

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