Importancia de la Bioequivalencia y la función del Sistema de Clasificación Biofarmacéutica

Ismael J. Hidalgo, Ph.D.

Absorption Systems
PANAMA

A **generic drug** (generic drugs, short: generics) is a drug defined as "a drug product that is comparable to a brand/reference listed drug product in dosage form, strength, quality and performance characteristics, and intended use."

Bioequivalence as proof of similar performance

The absence of a significant difference in the rate and extent to which the active ingredient in two pharmaceutical products reach the systemic circulation when administered at the same dose under similar conditions in an appropriately designed study

Why is it important to implement la Bioequivalence?

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Today the global generics market is $242 billions and growing

In the US generic drugs have been embraced as a way to control health care costs

In many Latin American countries, and Japan, generic drugs account only for 20% or less of total prescriptions

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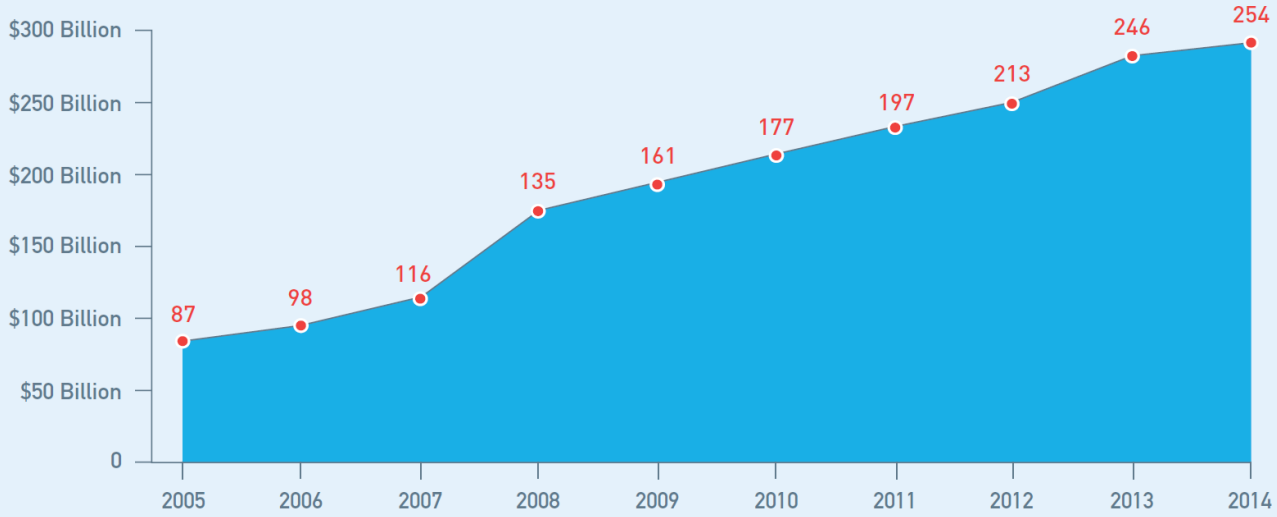
ANNUAL GENERIC DRUG SAVINGS IN THE UNITED STATES



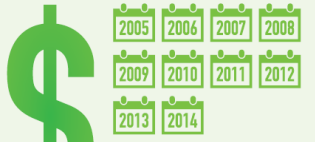
Historic savings have been revised to include standard data restatements.

GENERIC DRUGS IN THE UNITED STATES

88% OF PRESCRIPTIONS
but only 28% of drug costs

3.8 BILLION
PRESCRIPTIONS

254 BILLION SAVINGS



1.68 TRILLION
10-YEAR SAVINGS
(2005 - 2014)

Establishing Bioequivalence (BE)

Under FDA regulations, an applicant must use “the most accurate, sensitive, and reproducible approach available ….. to demonstrate BE.

in vivo and/or in vitro methods can be used to establish BE.

Descending order of preference: pharmacokinetic, pharmacodynamic, clinical, and in vitro studies.

Clinical Studies

Cost

Time

Adverse drug reactions

- Accidents with sleep inducers
- CNS drugs

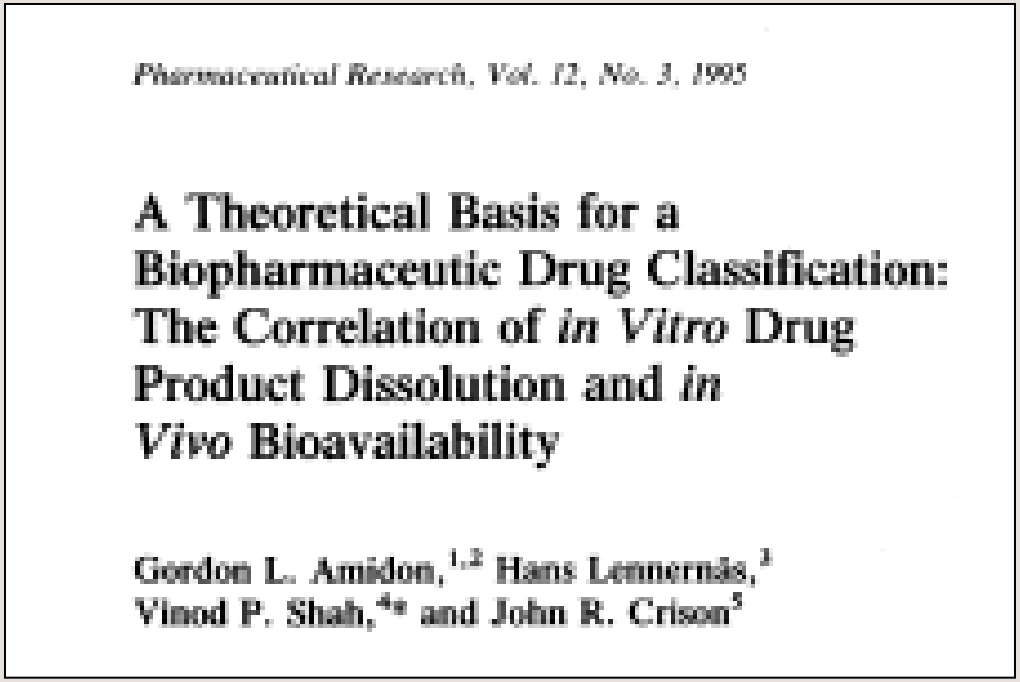
Special patient populations

- Cytotoxic and cytostatic drugs
- Steroids

Highly variable drugs

- Increased probability of Type I error in the clinic

Basic Principle Published in 1995



Pharmaceutical Research, Vol. 12, No. 3, 1995

A Theoretical Basis for a Biopharmaceutic Drug Classification: The Correlation of *in Vitro* Drug Product Dissolution and *in Vivo* Bioavailability

Gordon L. Amidon,[1,2] Hans Lennernäs,[3] Vinod P. Shah,[4*] and John R. Crison[5]

Amidon, G et. al. Theoretical Basis for a Biopharmaceutic Drug Classification: The Correlation of In Vitro Drug Product Dissolution and In Vivo Bioavailability, *Pharm Res* (12), 1994.

BCS Guidelines

Guidance for Industry

Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System

DRAFT GUIDANCE

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2015
Biopharmaceutics

Revision 1

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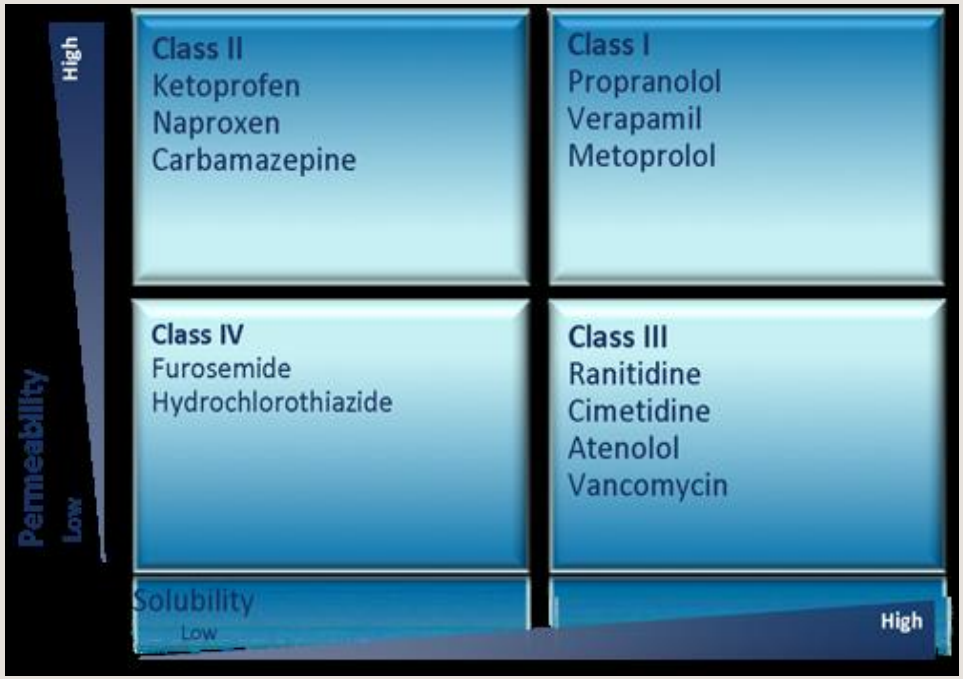
BCS Framework

1. If 2 drug products containing the same drug have the same concentration-time profile at the intestinal membrane surface, they will have the same rate and extent of absorption

2. If two drug products have the same in vivo dissolution profile under all luminal conditions, they will have the same rate and extent of drug absorption



Potential Waiver Candidates

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Grouping	Percentage of drugs by BCS class			
	Class I	Class II	Class III	Class IV
Top 200 in USA	34	33	26	7
Top 200 in Great Britain	33	33	27	7
Top 200 in Spain	32	27	30	5
Top 200 in Japan	36	36	20	7
WHO Essential Medicines List	34	19	38	10
Median	**34**	**30**	**29**	**7**

J. Cook et al Mol. Pharm. 4:1539-44, 2010

63%

BE Studies

Number of BE studies per year: 84 - 167

Typical number of subjects per study: 32

Typical cost: $220,000/study

	Maximum BW use
Studies waived	105
Subjects not used	3400
Money saved ($ millions)	34

J. Cook et al Mol. Pharm. 4:1539-44, 2010

In Vivo BE Studies:

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Bioequivalence of Oral Products and the Biopharmaceutics Classification System: Science, Regulation, and Public Policy

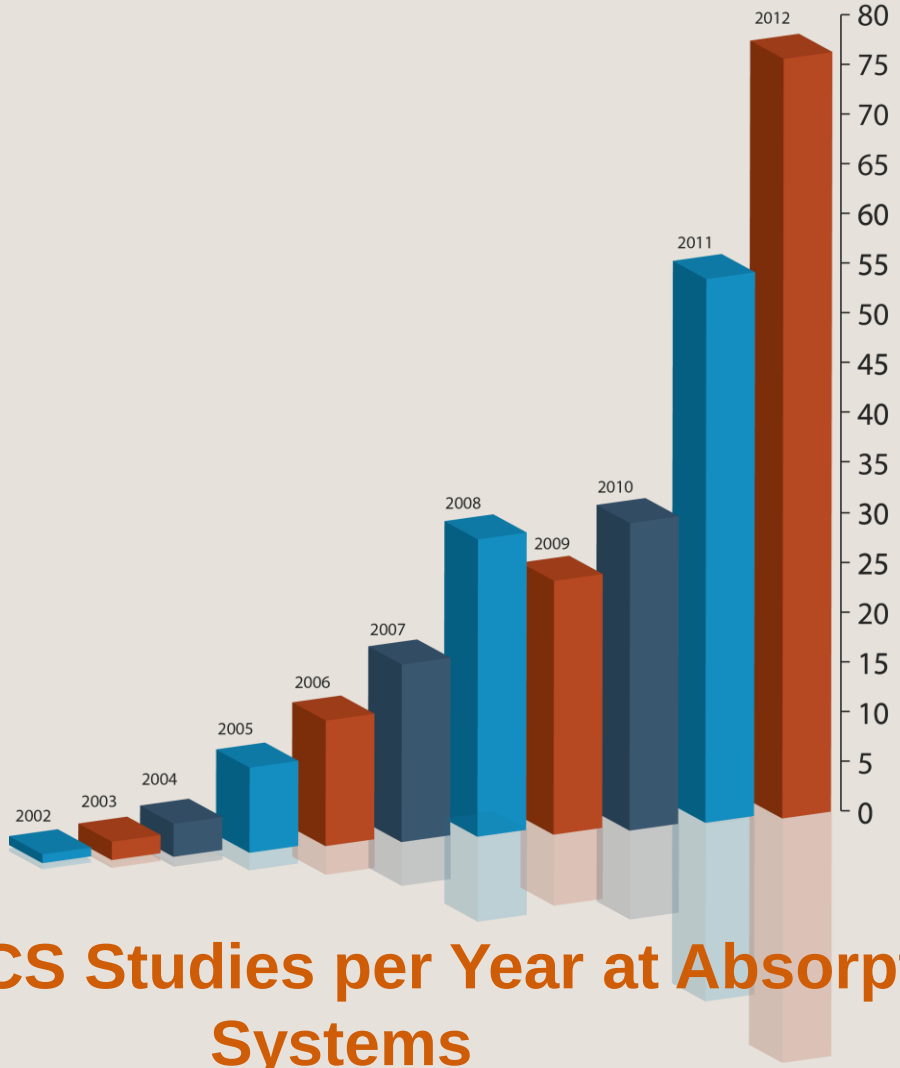
Clin Pharmacol Ther. 90: 467-470, 2011

KS Amidon, P Langguth, H Lennernäs, L Yu, and GL Amidon

"Although in vivo studies in humans are extensively used to document BE, they should no longer be viewed as the only type of evidence that can be used to establish the BE of oral drug products."

INCREASING ACCEPTANCE OF BCS

50+ ANDA Approvals with US FDA



Number of BCS Studies per Year at Absorption Systems

How to implement BE in LatAm?

Bioequivalence is necessary to ensure quality, efficacy and safety of generics

BCS is the only realistic approach that can bring effective and safe in vitro bioequivalence tests within reach for most local and regional manufacturers