BACKGROUND FOR ICH M10

Introduction

31-July-2019

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DISCLAIMER

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Regulatory History

WHERE DID IT START & HOW DID WE GET HERE

- 1972/78/81 New Zealand and Denmark/USA/OECD enact GLPs
- 1990 Crystal City I – establishes basic framework
- 1992 Health Canada - Guidance for Industry: Conduct and Analysis of Bioavailability and Bioequivalence Studies
- 2001 USA: FDA Guidance for Industry: Bioanalytical Method Validation
- 2003
  - USA: FDA Bioavailability and Bioequivalence Studies for Orally Administered Drug Products
  - Brazil: Resolution No. 899, Guide for Validation of Analytical and Bio-Analytical Methods
- 2005
  - India: Ministry of Health and Family, Guidelines for Bioavailability and Bioequivalence Studies
  - China: CFDA Technical guideline for human bioavailability and bioequivalence studies on chemical drug products
- 2009 International: WHO Good Clinical Laboratory Practice (GCLP)
- 2010 European Union: EMA Guideline on the Investigation of Bioequivalence
- 2011
  - China: CFDA (2011) Guidance on Management of Laboratory for Drug Clinical Trial Biological Sample Analysis
  - European Union: EMA Guideline on Bioanalytical Method Validation

Regulatory History

WHERE DID IT START & HOW DID WE GET HERE

- 2012
  - Brazil: ANVISA Resolution RDC 27, Minimum requirements for Bioanalytical Method Validation used in studies with the purpose of registration and post-registration of medicines
  - Canada: HPFB Conduct and Analysis of Comparative BA Studies
  - European Union: EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples
- 2013 Japan: MHLW Guideline on Bioanalytical Method Validation in Pharmaceutical Development
- 2014 Japan: MHLW Guideline on Bioanalytical Method (Ligand Binding Assay) Validation in Pharmaceutical Development
- 2015
  - European Union: EMA provides guide for reviewers that highlights the absence of US FDA laboratory certification process for GLP studies storage container
  - Canada: Health Canada requires stability testing to use 3 separate samples derived from separate containers, as opposed to 3 samples from a single tube
- 2016 China: NMPA: Guidelines on Bioanalytical Method Validation in China
- 2018 US: FDA revised Guidance for Industry: Bioanalytical Method Validation

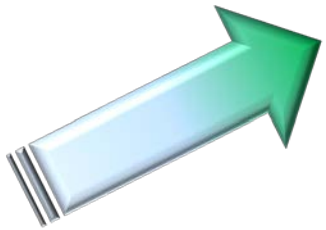
Growth in Regional Regulations Drove Call for ICH Guidance

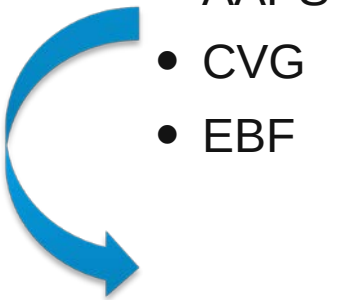
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 ?

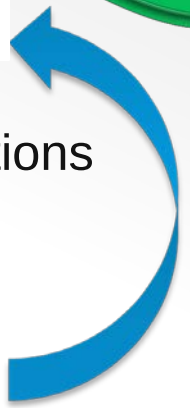
Industry Activities

COPING WITH REGULATORY CREEP AND REGIONAL DIFFERENCES

- Regional organizations
  - AAPS
  - CVG
  - EBF







- Spawned additional regional organizations
  - ACBio
  - APA India
  - CBF
  - JBF

Call for Harmonization

COPING WITH REGULATORY CREEP AND REGIONAL DIFFERENCES

Open Letter to FDA and EMA

- February 2010
- From EBF, AAPS, APA and CVG
- Request for Global Harmonization of the Guidance for Bioanalytical Method Validation and Sample Analysis
    - Calls for Consistency & Science-based regulations

The Call for Science and Consistency to ICH

BY 2015, MULTIPLE PEOPLE AND ORGANIZATIONS CONCERNED

Coping with regulatory scope creep and regional differences had expanded

- MHLW/PMDA submitted a proposal to ICH
- BI submitted a proposal and then withdrew in favor of one from the AAPS, European Bioanalysis Forum (EBF) and Japanese Bioanalysis Forum (JBF)
  - Submitted through EFPIA

October 2016, ICH announces M10 Concept Paper

ICH M10 Harmonized BMV

WHO HAS BEEN INVOLVED

Regulatory Members

- EMA, Europe
- FDA, US
- MHLW/PMDA, Japan
- Health Canada, Canada
- Swissmedic, Switzerland
- ANVISA, Brazil
- CFDA, China
- HSA, Singapore
- MFDS, Republic of Korea
- TFDA, Chinese Taipei
- WHO

Industry Members

- EFPIA
- JPMA
- PhRMA
- BIO
- IGBA
- WSMI
- IFPMA

PIC/S

OBSERVERS

- Standing Observers
- Legislative or Administrative Authorities
- Regional Harmonisation Initiatives (RHIs)
- International Pharmaceutical Industry Organisation
- International Organisation regulated or affected by ICH Guideline(s)

Expert Working Group Members

ICH Process and getting to a Finalized M10

A LOT HAS BEEN ACCOMPLISHED, MUCH MORE WORK TO COME

Step 0 **Proposal submission and acceptance**

ICH M10: Draft Guideline

Finalized ICH M10-

- Replaces regional guidelines/guidance of participants

Advantages

- One document for “all”
  - “Global” discussion of bioanalytical method validation
  - Common language
  - Same expectations
  - Fewer regional discrepancies

ICH M10: The Purpose

Recommendations for the validation of bioanalytical assays for chemical and biological drug quantification and their application in the analysis of study samples.

It is **NOT** an academic treatise on the science of bioanalytical method validation.

It describes the minimum expectations for the bioanalytical method validation of the studies you submit to support your regulatory application.

NOT in SCOPE: Biomarkers or immunogenicity

ICH M10: The Purpose cont'd

The objective of the validation of a bioanalytical assay is to demonstrate that it is suitable for its intended purpose.

Why is this so important?

- The concentration measurements of chemical and biological drug(s) and their metabolite(s) in biological matrices are an important aspect of drug development.

- Well characterised, appropriately validated and documented bioanalytical methods ensures the reliability of data used to make and/or support regulatory decisions about safety & efficacy (and labelling).

ICH M10: The Scope

Regulatory Submissions: INDs, NDAs, BLAs, ANDAs

What is it Applicable to?

- Chemical drugs (small molecule)
- Biological drugs(large molecules; therapeutic proteins; mAb, fusion proteins, enzyme replacement therapies etc.)
- Parent
- Active analytes/active metabolites

What kinds of studies?

- Nonclinical and clinical
  - Pharmacology/toxicology
  - Toxicokinetics/Pharmacokinetics

Responding to the Draft

AAPS, EBF AND JBF SISTER MEETINGS

Developing Regional and Global Responses

- Enable discussions by the scientific community on points of agreement and disagreement
  - Generate recommendations

- For Example
  - The Scope
    - Which studies are covered by the guidance
    - Define differences in requirements for the different ‘tiers’ of studies
    - Which studies are pivotal

Pivotal

EXPANDING COVERAGE

2001 FDA BMV

- Bioequivalence studies required the most extensive level of validation

2011 EMA BMV

- Bioequivalence studies labeled as pivotal

2018 FDA Revised BMV

- Additional studies added to the category of pivotal

2019 ICH M10 *DRAFT* BMV

- Further broadening of the studies that are considered pivotal

It's been difficult to get a clear definition

Industry has some proposals

Today

AGENDA

Outcomes of Regional Discussions

10:00 – 10:45 am	EBF Small Molecule View	*Philip Timmerman (EBF)*
10:45 – 11:00 am	Coffee Break	
11:00 – 11:45 am	EBF large molecule view	*Jo Goodman (MedImmune)*
11:45 – 12:00 pm	Q & A	
12:00 – 1:15 pm	Lunch	
1:15 – 2:00 pm	AAPS small molecule view	*Steve Lowes (Q2 Lab Solutions)*
2:00 – 2:45 pm	AAPS large molecule view	*Boris Gorovits (Pfizer)*
2:45 – 3:00 pm	Coffee Break	
3:00 – 4:00 pm	Roundtable	