Good Review Practices—A Common Regulatory Language—Influenced by the CTD

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Harmonization in Drug Regulation

Process of integrating national standards with international standards to be universally acceptable to participating countries to facilitate efficient global drug development and local registration

✦ Technical and science requirements
✦ Format and content of dossiers
✦ Assessment and review practices
ICH
INTERNATIONAL CONFERENCE ON HARMONIZATION
of Technical Requirements for the Registration of Pharmaceuticals for Human Use

http://www.ich.org
Hosted by ICH Secretariat
IFPMA-Geneva, Switzerland
A Unique Approach

• ICH was created in 1990

• Agreement between the EU, Japan and the USA to harmonize different regional requirements for registration of pharmaceutical drug products
  – Canada, EFTA and WHO participate in ICH as observers

• Unique because joint effort by regulators and associated pharmaceutical industry trade associations (includes Generics and OTC)

• Pharmaceutical industry aware of areas of disharmony in regulatory submission requirements
ICH Harmonized Guidelines

- **Efficacy** - 15 topic headings/19 guidelines
- **Safety** - 9 topic headings/14 guidelines
- **Quality** - 10 topic headings/33 guidelines
- **Multidisciplinary** (Regulatory Communications)
  - Medical Dictionary - MedDRA
  - Electronic Standards - ESTRI, E2B, eCTD

- In 1996 ICH industry representatives proposed assembling the information generated by these harmonized guidances in the same order
- Goal was to decrease the amount of time and staff needed to assemble and disassemble documents for submission to ICH regions
# Table of Contents Comparison

**New Drug Application**  
U.S.A.

- List of Investigators: 8.A
- Overview of Clinical Investigators: 8.B
- Clinical Pharmacology: 8.C
- Controlled Clinical Studies: 8.D
- Uncontrolled Clinical Studies: 8.E
- Other Studies, information: 8.F
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- Drug Abuse, Overdose info.: 8.I
- IS if Benefits, risks: 8.J
- Compliance: 8.K
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- Statistical info.: 10.

**E.U. MA Application**

- Part IC3: Expert Reports
- Part IVA: Clinical Pharmacology
- Part IVB: Clinical
- Part IVQ: Other
- Part IB1: SPC

(Human PK, BA also in Part 6 of US NDA)
Concerns

• Regulators realized the amount of time and energy needed to rearrange paper from one ICH region submission format to another
• Conversion caused a delay in submitting an application to that ICH region
• Resulted in delayed access to new innovative medicines for patients in that region
ICH CTD

1.0 Regional Administrative Information
1.1 ToC of Module 1 or overall ToC, including Module 1

2.1 ToC of the CTD (Mod 2,3,4,5)
2.2 Introduction
2.3 Quality Overall Summary
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Summary
2.7 Clinical Summary

Source: ICH Implementation Coordination Group
Benefits of the CTD--FDA Perspective

- More *reviewable* applications
  - More logical order of presentation
  - Follows development scheme
- More predictable format
- More consistent reviews
- Easier analysis across applications
- Easier exchange of information
- Facilitates electronic submissions
eCTD Format and the Review Process

Easier to Develop Standardized Reviewer eTemplates
Promotes eSubmission and eReview tools
Harmonized Submissions Promote Better Reviews

- Increased international harmonization efforts demands an understanding of what we do and expect to be submitted from industry
- Reviews need to consistently and successfully communicate complex technical information in response to industry’s submissions
- Therefore harmonization has encouraged the development of high-quality reviews
Guidance to Industry → GRPs

• It should be appreciated that what we believe we should do in a review is closely tied to what data we want a sponsor to submit.

• As a result, there will be considerable similarity between guidance to industry and what we consider good review practices.

• Because ICH Regions have harmonized much of the information submitted for marketing authorization, ICH regulators could trend towards similar review practices.
Smart Program, DFS, EES, OTCOM Established

Reviews Evaluation Project - Draft ISS Guidance

Reviews Evaluation Steering Group - renamed - Reviews Evaluation & Education Project

GRP Clusters 1-5 Begin*

1995

1996

1997

1998

*The Clusters
1 - Define Good Review
2 - Obtain Buy-in
3 - Implementation
4 - Training
5 - Impact/External Evaluation

2000

CTD Finalized

2001

Review Templates

Pharm/Tox Review Format - Draft Guidance

Good Review Practices
CDER’s GRPs

• Maintain that it wasn’t until the CTD was finalized in 2000 that the goal of GRPs could be realized
• GRPs required a predictable submission format to create the review templates necessary for consistency
  – April 2001—CDER launched the General Clinical Template
  – October 2002—Six additional templates issued
    • Pharm/tox, biometrics, clinical microbiology, chemistry, clinical pharmacology/biopharm, microbiology
• Templates were intended to standardize the order and placement of topics within a review
• Templates are generally based on the CTD
Influence of the CTD on GRP

• The CTD format of a submission influences content by imposing a logic to the review
• The CTD builds in function by shaping both the conduct of the review and the presentation of the results of the review
• The influence of the CTD on review will most likely spread throughout ICH and non-ICH regions as regulators apply GRPs to their review process
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ICH Working Groups

Complementary
ICH Global Cooperation Group

- Created in 1999 to address increasing interest by non-ICH parties in ICH guidelines and operations
- Initial focus on information-sharing
- Soon became clear that more active engagement was necessary to respond to increasing interest in ICH and ICH guidelines
- Invited participation of regional pharmaceutical harmonization initiatives
Regional Harmonization Initiatives

- APEC – Asia-Pacific Economic Cooperation
- ASEAN – Association of the Southeast Asian Nations
- GCC – Gulf Cooperation Council
- PANDRH – Pan American Network for Drug Regulatory Harmonization
- SADC – Southern African Development Community
Expanded GCG
ICH Meetings June 8-12, 2008

- Participation of individual countries for first time
- Distinct and complementary to participation of official RHI representatives
- Expansion of GCG to specific countries based on considerations such as:
  - Source of APIs, medicinal products and clinical data for ICH regions
  - Use or intended use of ICH guidelines
Expanded GCG
Invitations Extended to Individual Drug Regulatory Authorities

- Australia
- Brazil
- China
- Chinese Taipei
- India
- Korea
- Russia
- Singapore
Regulators Forum

• Met for the first time prior to ICH meetings in Portland, June 9, 2008
• Created to promote discussion and sharing of best practices among regulatory authorities on issues related to the implementation of ICH guidelines and impact on regulatory systems
• The Regulators’ Forum complements activities and objectives of GCG
Efficient Transfer of Information

CTD, GCP, GMP, PCV, GRP
Conclusion

- The geographical face of international drug development and trade is rapidly changing.
- Interest and use of ICH guidelines by non-ICH countries reflects this change.
- Use of ICH guidelines will promote Good Review Practices and increased interactions between DRAs and hopefully increased access to safe, effective and quality pharmaceuticals worldwide.
Thank you for your attention