

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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Date: November 26, 2002  
To: Dockets Management Branch (HFA-305)  
From: Lafayette Gross  
Office of Generic Drugs  
Subject: Division of Bioequivalence Update

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

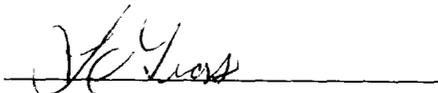
Title of Presentation: Division of Bioequivalence Update

Presented for: GphA Fall Technical Workshop

Date Presented: October 15, 2002

Presented by: Dale P. Conner  
Division of Bioequivalence, OGD

Number of Pages: 16



Attachment

90S-0308

M 728

# Division of Bioequivalence Update

GPhA Fall Technical Workshop

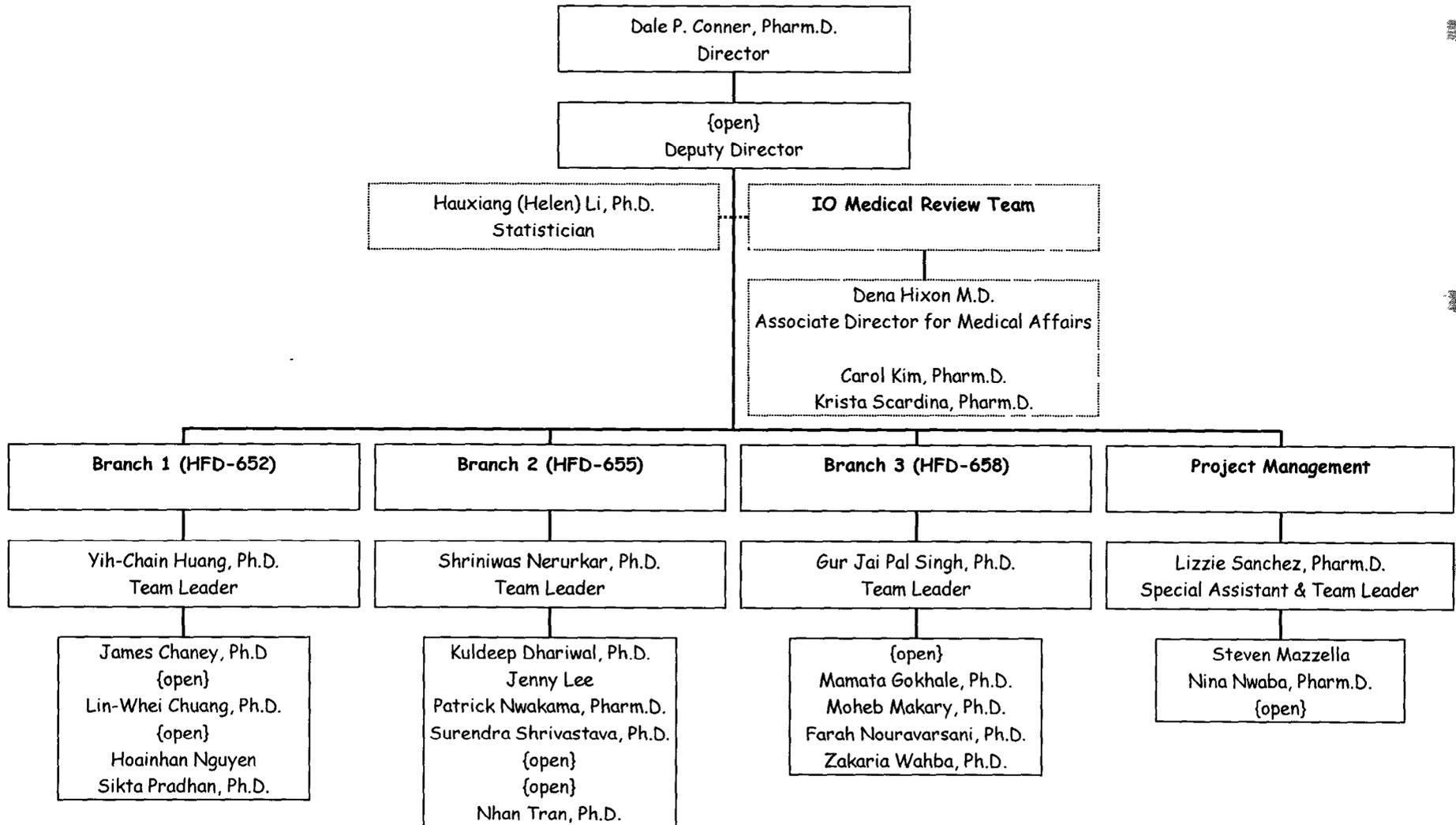
Dale P. Conner

Division of Bioequivalence, OGD

# Introduction

- Structure of Division of Bioequivalence
- Various BE Issues/Questions

# Division of Bioequivalence



# Current DBE Backlog

- Control Documents
  - Duplicates
  - Multiple products in single document
  - Lower priority than ANDAs
- ANDA
  - Queue

# New Review Format

- • Center initiative to standardize review formats
- • DBE is currently developing review template
  - Standardize review format
  - Streamline completion of review documents by reviewers
  - Make future information retrieval more efficient
- • Data should be submitted in SAS Transport

# Guidances

- Good Guidance Practices (GGPs) 21 CFR 10.115
- Comments can be submitted at any time to any guidance
- Guidances can be drafted and submitted for consideration by interested parties

# Guidances

- BA/BE
- Fed BE
- Clozapine
- Topical Antifungal
- Nasal Products

# Replicate Design vs. Two-Way Crossover

- Current general BA/BE guidance recommends replicate design for MR products
- New draft guidance changes this recommendation
- Either design is acceptable
- Analysis is by average BE

# Reserve Sample Retention

- 21 CFR 320.63 and 21 CFR 320.38
- Continues to be a problem
- Problems frequent in bioequivalence studies with clinical end-points
- Clinical investigator should choose test article samples for retention
- Draft guidance published for comment

# Food-Effect BE Studies

- Currently
  - If a food effect (even a negative one) on bioavailability is mentioned in the labeling a fed BE study should be submitted
  - If the labeling instructions say to **ONLY** take on an empty stomach then a fed BE study is not necessary

# Food-Effect BE Studies

- Currently
  - Two-way crossover studies
  - Point estimates should fall within 80 - 125%
  - No waivers of fed-BE studies for BCS Class 1 drugs (yet)
- Draft Guidance
  - 90% Confidence interval criteria
  - BCS waivers for fed BE studies for Class 1

# Date of Implementation of Guidances

- Date may be stated in the guidance
- If not stated it is usually on the date of issuance of the final copy
- If you have a pending deficiency and a new guidance seems to say that this is no longer a deficiency -- consult the appropriate review division

# Biopharmaceutics Classification System (BCS)

- Few ANDA submissions
- Almost none contain permeability data performed by sponsors
- Literature data?
- FDA has tentative plans to classify some compounds

# “Failed” Studies

- Agency is requesting submission of “failed” or additional studies
- Studies on the “final” formulation
- These studies to be submitted as complete summaries
- Clarification of regulations is planned
- Guidance is also planned after regulation changes are finalized

# Pharmacokinetic Reassays

- Reassay of samples for “pharmacokinetic” reasons
- This is discouraged, but if you do it
- Objective a priori criteria should be stated in SOP
- Provide a complete before and after data analysis

# In Vitro Dissolution

- - Provide laboratory site information
  - DSI inspections are planned
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