

Table of Contents

Dr. Sharlin's Credentials	4
Outline of This Presentation	5
History of ISE Requirements and Recommendations	6
Differences between the 1988 and 2008 ISE Guidances.....	7
ISE Requirements for an NDA in 21 CFR 314.50(d)(5)(v)	8
Five Required Elements of ISE Content.....	9
Five Required Elements of ISE Content (page 2)	10
Five Required Elements of ISE Content (page 3)	11
ISE is a Recommended Part of a BLA	12
The ISE is Not a Summary	13
Locate the ISE in CTD Module 5 (Clinical Study Reports).....	14
Locate the ISE in CTD Module 5 (page 2).....	15
For Small Studies, the ISE Could Be Split between CTD Modules 5 and 2 (CTD Summaries)	16
In A Paper Submission, Place the ISE in Clinical & Statistical Sections	17
Information Reviewers Require For a Statistical Review, MAPP 4000.8	18
Information Reviewers Require For a Clinical Review, MAPP 6010.3	19
ICH Guidances Related to the ISE	20
Tables and Figures in an ISE	21
What the ISE Should Not Contain.....	22
Seven ISE Sections	23
ISE Section 1 of 7 -- Background and Overview of Clinical Efficacy	24
ISE Section 2 of 7 – Tabular Results of Individual Studies	25
ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies	26
ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies (page 2)	27

ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies: (1)
Demographic & Baseline Characteristics of Efficacy Study Populations (pg 3).....28

ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies: (2)
Efficacy Results (page 4).....29

ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies: (3)
Analysis Issues (page 5)30

ISE Section 3 of 7 – Comparisons and Analyses of Efficacy across Studies: (4)
Integrated Data Analyses (page 6).....31

ISE Section 4 of 7 – Comparison of Results in Subpopulations32

ISE Section 4 of 7 – Comparison of Results in Subpopulations (page 2).....33

ISE Section 5 of 7 – Analysis of Clinical Information Relevant to Dosing
Recommendations.....34

ISE Section 6 of 7 – Persistence of Efficacy and/or Tolerance Effects35

ISE Section 7 of 7 – Exploratory Investigations36

Checklist: Mapping ISE Content into the CFR37

Summary and Conclusions from this Teleconference.....38

Next Steps39

Joshua Sharlin, Ph.D., Resume.....40