

Nonclinical evaluation for anticancer pharmaceuticals - Step 4 -

International Conference on Harmonisation of Technical
Requirements for Registration of Pharmaceuticals for Human Use



Guidance Development

■ S9 Guidance Timeline

- Business plan proposed by US PhRMA
- Endorsed by ICH Steering Committee May 2007
 - Driver for guidance:
 - separate regional oncology guidances were being developed
 - in the absence of an oncology guidance, recommendations outlined in ICH M3 and S6 were being requested
- First meeting Yokohama Japan Oct 2007
 - Japan, EU, and US discussed current and proposed approaches to anticancer drug and biological development

■ Milestones

- Additional meetings Portland OR (June 2008); Brussels (Nov 2008); Yokohama (June 2009)
- Planned release:
 - Step 2: October 2008
 - Step 4: Oct 2009

Guidance Development

■ ICH:

- ICH S9 Step 2 guidance document is available from the ICH website (ICH.org).

■ Status

- Public comment period closed earlier this year
- Approximately 215 comments received
- Comments discussed in Yokohama in June 2009
 - EWG revised the Step 2 document
- EWG completed discussions to reach Step 4
- The document provides clarity in recommendations to facilitate regional implementation

Prior Accomplishments

- Approaches to setting a safe start dose for clinical trials
- Study design to support initial clinical development
- Duration of repeated dose toxicity testing limited to 3 months
 - Available prior to phase 3
- Reproduction toxicology requirements to only embryo-fetal toxicology assessment
 - Not essential for pharmaceuticals that target rapidly dividing cells

Update on Accomplishments

- Agreement on language of scope
- Agreed on flexible approach to safety evaluation of metabolites and impurities relative to available regional and ICH guidance
- Agreement on the scientific discussion on need for recovery groups
- Agreement on photosafety testing appropriate to the patient population
- Agreement on studies to support pharmaceutical combinations
- Step 4 reached ahead of the business plan timeframe

Accomplishments

- In all discussions the 3 R's were kept in focus to ensure the goals in the concept paper are followed
- Identified areas of other guidance that can be used to reduce possible future maintenance, e.g. use of S6 for biopharmaceuticals testing
- Accepted by FDA legal review without substantial revision

Members of ICH S9 EWG

■ EU

- Klaus Olejniczak - BfArM –TL
- Mikael Andersson – MPA – DTL
- Ulla Wändel-Liminga – MPA – Expert (July 2009 – present)
- Hermann Schweinfurth - Bayer Schering Pharma - TL
- Marco Brughera - Nerviano Pharmaceuticals - DTL

■ •Japan

- Hiroshi Onodera - MHLW/PMDA -TL
- Osamu Fueki - MHLW/PMDA - DTL
- Dai Nakae - MHLW - Expert
- Shuichi Kai – Bristol-Myers – TL
- Chihiro Nishimura – Nippon Kayaku - DTL
- Atsushi Sanbuissho – Daiichi Sankyo – Expert (To July 2009)
- Takahiro Nakazawa – Eli Lilly – Expert (To July 2008)

Members of ICH S9 EWG

■ USA

- John Leighton - US FDA CDER–TL/Rapporteur
- Mercedes Serabian - US FDA CBER - DTL
- Ann Pilaro - US FDA CDER - Expert
- Daniel Lapadula - Novartis TL
- Vijayapal Reddy - Eli Lilly – DTL

■ Observers

- James Green - Biogen – BIO
- Helen Mao - Health Canada (To July 2009)
- Tatiana Lejen - Health Canada (July 2009-present)
- Beat Schmid – Swissmedic

■ Others

- David Jacobson-Kram and Joseph DeGeorge

- And many thanks to colleagues in our organizations that contributed to the development of the guidance