BioSafe

Introduction and rare disease activities

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Disclaimer

The opinions expressed in this presentation reflect those of the presenter(s) (or speaker(s)) only and do not necessarily represent the views of the Biotechnology Industry Organization (BIO) or any other person in, or member of, BIO.
Who are we –

- Representatives from pharmacology, toxicology and regulatory departments from biopharmaceutical organizations large and small
- Founded in 2003, Joy Cavagnaro
- 17 Leadership Committee members + ex officio members
- Three Expert Working Groups
- Approximately 300 General Membership members
- Mission – “to serve as a resource for BIO members and BIO staff by identifying and responding to key scientific and regulatory issues related to the preclinical safety evaluation of biopharmaceutical products”
Our scope – “biopharmaceuticals”

- Enzymes
- Growth factors
- mAbs
- Gene therapies
- Cell therapies
- Vaccines
- Combining modalities
  - ADCs
  - Targeted T-cells
- Nucleic acids
- Plasma and recombinant blood products
Biosafe Intro

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How do we test all these?
What types of studies?
How long?
In vitro or in vivo?
What species?
Our notable accomplishments

- Member of International guidance Working Parties
- Published white papers addressing
  - Chronic toxicology assessment of biopharmaceuticals
  - Carcinogenicity assessments for biopharmaceuticals
  - Tissue Cross Reactivity assessments for biopharmaceuticals
  - Alternative testing models for biopharmaceuticals
  - Immunogenicity assessment of biopharmaceuticals
  - Placental transfer of biopharmaceuticals
  - Development of antibody-drug conjugates
  - Appropriate assessment of biodistribution for gene therapies
  - First in human dose selection for biopharmaceuticals
  - Reproductive toxicology for biopharmaceuticals
  - Support for pediatric clinical studies for biopharmaceuticals
  - Toxicology of PEGylated biopharmaceuticals – in progress
  - Comparability assessments for biopharmaceuticals – in progress

Biosafe Intro
What are we up to?
- Annual general membership meetings in US and EU
- Interaction with regulatory authorities
  - FDA – CDER and CBER
  - China-FDA
  - EMA
- Commenting on and participation in forming guidance
  - Several FDA and EMA guidance documents
  - Participation in upcoming international guidances (ICH-S9, -S5, -S3, Juvenile toxicology, Vaccines)
- Webinars
What are we up to?

- Topic working groups
  - Optimizing animal usage and alternative testing strategies
  - PEG
- Expert working groups
  - Specialty biologics
    - Gene/Cell Therapy
    - Vaccines
    - Blood
  - PK/PD
  - Mechanisms of action
Where are we going?

- Expanding our regulatory scope
- Keeping pace with “advanced therapies”
- Advocating responsible animal usage and reliable alternatives to animal studies
- Advocating for targeted approaches for IND-enabling safety assessment for rare disease therapies
Biosafe annual meeting with CDER
July 30, 2014

- Four nonclinical topics addressed
- Rare disease session
  - Organized by Laura Andrews - Abbvie
  - Presentations by
    - Chuck O’Neill – Biomarin
    - Joy Cavagnaro – AccessBIO
    - Dennis Schrier – Alexion
    - Lee Silverman – Agios
    - David Joseph – FDA
- Meeting in conjunction with IQ/DruSafe
Takeaways from rare disease session -

- An FDA review of chronic toxicology studies for enzyme replacement therapies found a few studies identified unique findings using normal animals.
- As a result, FDA still considers the 6mo chronic study relevant to ERTs, though the value is still under assessment.
- A strong push by industry to use animal models of disease, an approach historically promoted by CBER.
- Encouragement to apply principles of ICH S9.
Forming topic group to address challenges with preclinical aspects of rare diseases

Intention to publish position piece outlining the following –

- **For programs where human clinical data already exists via compassionate use or investigator initiated trials, such data should trump the need for animal safety data.**

- **For programs where no human data exists, short term (no longer than 3mo) preclinical safety studies should be sufficient to support first in human clinical trials.**

- **A defined guidance to for a novel approach to preclinical assessment of therapeutics for rare life threatening diseases should be considered at the health authorities or ICH level. In the interim, principles of ICH S9 should apply for preclinical safety testing in non-oncology rare life-threatening diseases.**
Intention to publish position piece outlining the following –

- *Preclinical juvenile toxicology studies should be conducted only when there is specific concern*

- *Toxicology endpoints obtained in animal models of disease, when available, should be sufficient for preclinical safety testing*

- *Reference should be made to the November 2013 CBER guidance on Preclinical Safety Testing for Gene/Cell Therapies and ICH S6 - principles within (animal models of disease in lieu of normal animal testing, non-GLP testing in certain circumstances) should apply to non gene/cell biologics for these rare life-threatening diseases.*

- Christopher Horvath – Bluebird Bio
- Laura Andrews – Abbvie
- Joy Cavagnaro – AccessBIO
- Tim MacLachlan – Novartis
- Lauren Black – Charles River Laboratories
Leadership Committee

- Tim MacLachlan, Novartis
- Marque Todd, Pfizer
- Jim Green, Boehringer-Ingelheim
- David Hutto, Eisai
- Maggie Dempster, GSK
- Shawn Heidel, Covance
- Garvin Warner, Alnylam
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- John Vahle, Lilly
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- Rafael Ponce, Amgen
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- Jenny Sims, Integrated Biologix

Questions? Please contact –

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- Marque Todd (Marque.Todd@pfizer.com) - Biosafe Vice Chair
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- Reproductive toxicology for biopharmaceuticals (Martin PL, Birth Defects Res B Dev Reprod Toxicol 2009; 86: 176-203)
- Carcinogenicity assessments for biopharmaceuticals (Vahle JL, Toxicol Pathol 2010; 38: 522-53)
- First in human dose selection for biopharmaceuticals (Tibbits J, Regul Toxicol Pharmacol 2010; 58: 243-251)
- Tissue Cross Reactivity assessments for biopharmaceuticals (Leach MW, Toxicol Pathol 2010 38: 1138-66)
- Support for pediatric clinical studies for biopharmaceuticals (Morford Birth Defects Research (Part B) 2011 92:359-380)
- Development of antibody-drug conjugates (Roberts SA, Regul Toxicol Pharmacol. 2013 67:382-91)
- Comparability of biopharmaceuticals after manufacturing changes (Cavagnaro J, in preparation)
- Toxicology of PEGylated biopharmaceuticals (Ivens I, in progress)