



Major presentations at various Conference

Members from the working group have made more than 33 presentations at various conferences including JSM, DIA annual meeting, DIA Pharmacovigilance & Risk Management conference, Duke-Industry Statistics Symposium, DIA/FDA Biostatistics Industry and Regulator Forum, PHUSE, World Drug Safety Congress, etc.

More than 8 publications (including books were accepted/ published/ submitted as work from the working group



- Dr. Lothar Tremmel has been elected as the new co-chair and will start his 3-year tenure on Jan 1 2024. Mengchun Li, Jürgen Kübler and Lothar Tremmel will be the three co-chairs in 2024.
- We also want to thank Dr. James Buchanan for his wonderful leadership as a co-chair in the past three years
- Welcome to the Leadership Council team: Barbara Hendrickson, Michael Fries, Ellen Snyder, Lian Lin, Birol Emir and Michelle Zhang
- We also want to thank Dr. Bill Wang for his amazing leadership as WS3 co-lead in the past years

ASA Biopharma Safety Working Groups

Official Public
Private Partnership
(PPP) in place

US FDA

Work Stream 1#

Interdisciplinary
Safety Evaluation
(collaboration with DIA)

Work Stream 2

Safety Monitoring Statistical Methodology

Aggregate Safety Assessment

Planning (ASAP)

Interactive Safety Graphics (ISG)

Benefit Risk Assessment Planning (BRAP)

Benefit Risk Assessment Tool Suite (BRATS)

Work Stream 3

Integration and
Bridging RWE
and RCT for
Safety DecisionMaking

TF1:Statistical and design considerations for real world evidence in health decision making

TF2: Design and Analyses of the Pharmacoepi Studies

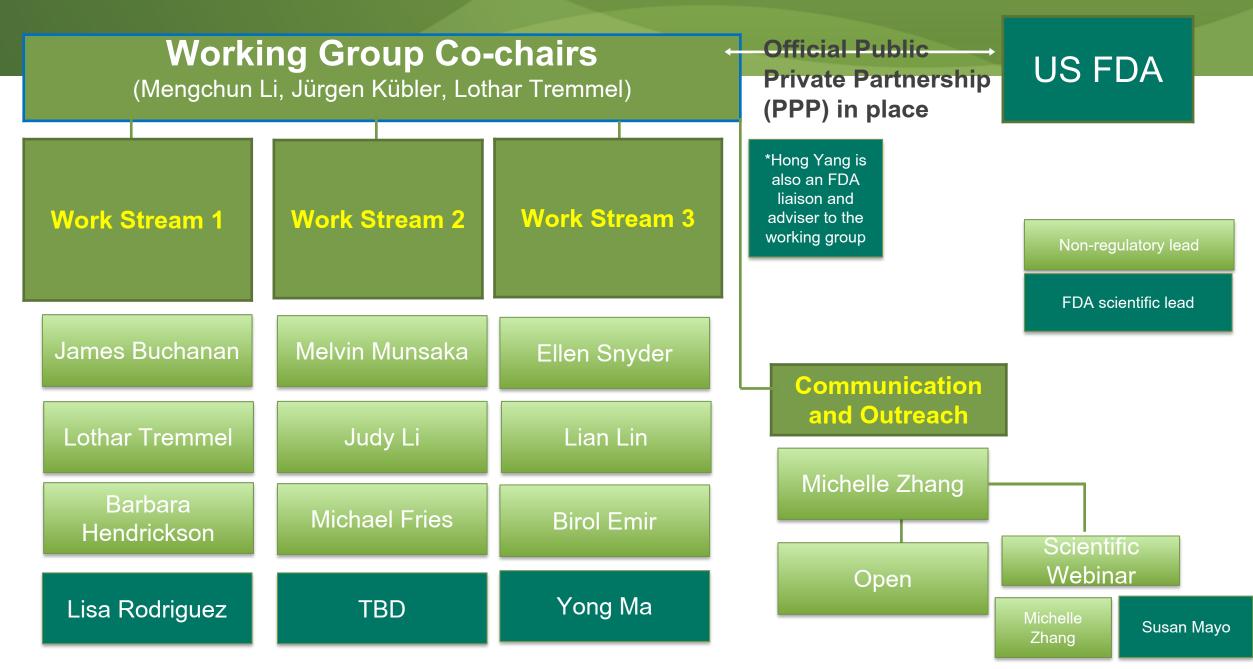
TF3: Advanced methods and analytics in application to RCT and RWE

Communication and Outreach

(Including quarterly Scientific Webinar)

Website of the working group: <u>Safety Scientific Working</u>
<u>Group - Biopharmaceutical Section (amstat.org)</u>

Leadership Team starting from Jan 2024



Important Notes

Membership survey and confirmation

- 2023 Year-End Member Satisfaction Survey (to be sent out in Jan 2024)
- Membership confirmation(NEW: active sign in required)

Year-end personal acknowledge

- If you want us to send your manager an acknowledgement email, please contact us with your request and send us your manager's email
- Please let us know before Dec 20



Leadership Team in 2023

Workstream 1 (co-leads: James Buchanan, Lothar Tremmel, Mengchun Li, Lisa Rodriguez)

BRATS ISG **ASAP BRAP** Mengchun Li Jeremy Wildfire **Lothar Tremmel** Brian Edwards Brian Barbara James Buchanan James Higginson Waterhouse Hendrickson Xiao Ni Lisa Rodriguez

Mengchun Li

Taskforce Non-regulatory lead

FDA scientific lead

Workstream 1 (co-leads: James Buchanan, Lothar Tremmel, Barbara Hendrickson, Lisa Rodriguez)

BRATS ISG **ASAP BRAP** Natalia Mengchun Li **Lothar Tremmel** Brian Edwards Andriychuk Brian Barbara James Buchanan James Higginson Waterhouse Hendrickson Xiao Ni Lisa Rodriguez

Mengchun Li

Non-regulatory lead

FDA scientific lead

Workstream 1 is the Interdisciplinary one

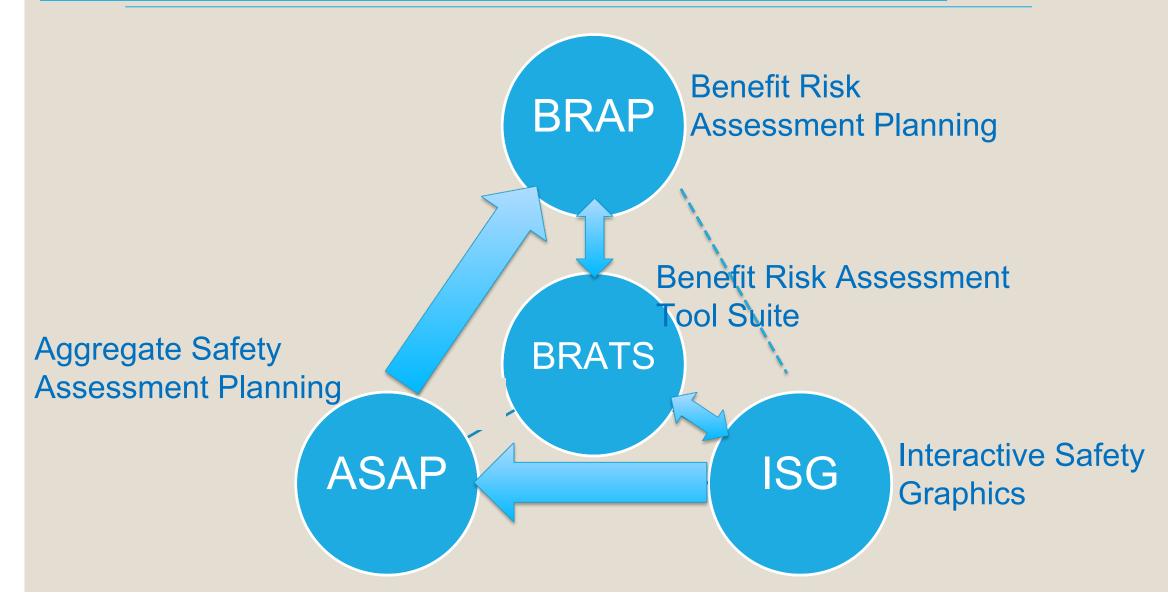
Goals

Bring together the various disciplines that are involved in establishing the safety

profile of new treatments:

- Epidemiology
- Statistics
- Medicine/clinical
- Pharmacology
- o and more...
- Address problems related to drug safety analyses that require interdisciplinary collaboration
 - o Focus is on pre-marketing safety, during clinical development

Inter-Taskforce Collaboration within WS1



Workstream 1 Taskforce 1: ASAP: 2023 Accomplishments

Presentations

Short Course, the DIA Global Pharmacovigilance and Risk Management Strategies Conference), January 2023

How ASAP supports ongoing signal detection, DIA GPRMS Conference, February 2023

Re-imagining a Safety Submission - PHUSE Community Forum, February 2023

How ASAP supports ongoing signal detection; DAISE Working Group Scientific Webinar, March 2023

How ASAP support Safety Topics of Interest; DIA Annual Meeting, June 2023

ASAP linkage with Interactive Safety Graphics, World Drug Safety Congress, October 2023

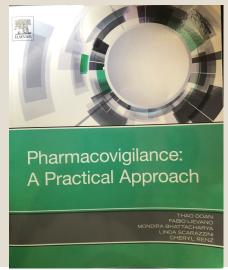
European PV Conference, December 2023

ASAP: Publications in 2023

Hendrickson, B.A., Agarwal, A., Bennett, D., Kübler, K., McShea, C. and Tremmel, L. Value and Implementation of the Aggregate Safety Assessment Plan. *Pharm Med* 37(3):171-181, 2023.

How the Aggregate Safety Assessment Plan supports IND Safety Reporting, in process (sumitted to TIRS, review in progress)

New Chapter in Textbook, Pharmacovigilance: A Practical Approach (originally published in 2018; being updated)



Future Focus for Task Force in 2024

- 1) Helping smaller companies implement the ASAP principles
- 2) Identification of anticipated events for the patient population and overcoming the obstacles of identification of event reference rates (co-effort with WS3)
- 3) Safety evaluation when using historical trial/registry data to support a new drug approval



Workstream 1 Taskforce 2: Benefit-Risk Assessment Planning (BRAP)



- New co-lead added (James Higginson)
- New members were added

BRAP: 2023 accomplishments

- Pivoted to best practices for BR planning deliverable to adjust to CIOMS WG XII Benefit-Risk Report
- Formed subgroup to focus on deliverable outline and planning (held 3 workshops so far and agreed on high level content)
- Forming additional subgroups to author sections of deliverable (for initiation of writing in 2024)
- Added project manager and CDRH clinician as members; removed inactive members from roster (see attached for most current membership list)
- Submitted two publications:
- Key Opinion Leaders Interviews to Inform the Future of Benefit-Risk Planning in the Medical Total Product Life Cycle of Global Pharmaceutical and Medical Device Organizations (submitted to Drug Safety)
- M Gebel, C Renz, L Rodriguez, A Simonetti, H Yang, B Edwards, JM Higginson, N Charpentier, M Colopy; "A survey to assess the current status of structured Benefit-Risk assessment in the global drug and medical device industry," submitted to Therapeutic Innovation & Regulatory Science

BRAP: 2024 Objectives

Manuscript on Points to Consider for Benefit-Risk planning

Get BR survey work published.



Workstream 1 Taskforce 3: ISG 2023 Accomplishments



Introduction to the ISG visualization tools and their value in identifying adverse effects and signal detection. DIA Pharmacovigilance & Risk Management conference. February, 2023

Signal Detection in Clinical Development – Importance of Aggregate Safety Assessment Planning, Including Usage of Interactive Safety Graphics (ISG) Tools. ASA Biopharm WG Scientific Webinar. March, 2023

QT Visualization for Clinical Trials: QT Explorer. ASA Biopharm WG Scientific Webinar. March, 2023

Ongoing Aggregate Safety Evaluation (OASE) as part of the ASAP Process – Leveraging the Power of Interactive Safety Graphics for Data Exploration. ASA Biopharm WG Scientific Webinar. March, 2023

Reimagining a Safety Submission. Presented March 2023 at Phuse Community Forum Webinar.

Augmented Intelligence: Leveraging Interactive Graphical Tools to Explore Safety Data. DIA Global Annual Meeting, June 2023

Overall Safety Assessment – Standard Safety Tables and Figures. Interdisciplinary Safety Evaluation for Learning and Decision-making Webinar Series. July 2023

Secrets to Pre-competitive Collaboration: Accelerating Open-Source in Clinical Trials, Sep 2023 at Fierce Clinical Summit in Philadelphia, PA.

Interactive Safety Graphics: Innovative Approaches to Safety Analytics, Oct 2023 at Phuse Safety Analytics Webinar Series.

Updates from the Drug Information Association–American Statistical Association Biopharmaceutical Safety Working Groups (Workstream One), World Drug Safety Congress, October 2023

The Interactive Safety Graphics Suite of Tools. ASA Biopharm WG Scientific Webinar. December, 2023

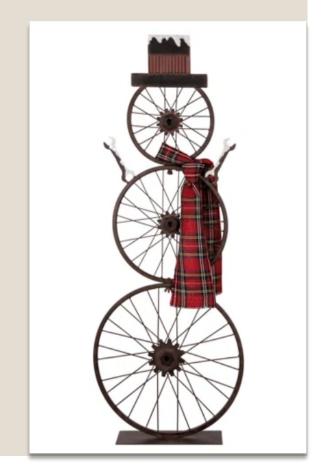
Key Takeaways from PHUSE 2023 Forums on Interdisciplinary Safety Evaluation, PHUSE Community Webinar, November 2023

AE volcano plot published on CRAN

Published Renal Explorer

ISG: 2024 Objectives

- Planned new feature (Patient Profile) for future update
- Further development of Renal Explorer, QT Explorer
- Beta testing and pilot of the tools with selected companies



BRATS Accomplishments 2023

- Drafted and received feedback on initial Value Tree (VT) App Yusuf Ali (FDA) and the VT tech sub-team;
 Q1-Q3, feedback received August 18, 2023
- Updated Forest Plot (FP) App Brian Waterhouse (Merck) and the FP tech sub-team; most recent review on August 18, 2023
- Shared experiences on software and/or approach for BR assessment from various companies
 - ∘ GSK Danae Williams; April 25, 2023
 - ∘ UCB Mike Colopy; June 26, 2023
 - AstraZeneca Jiyoon Park; October 23, 2023
- External presentations at
 - Quarterly scientific Webinar sponsored by the Scientific Working Group on CIOMS XII and SWG
 Response Hong Yang, Leo Plouffe, Lisa Rodriguez, and Mike Colopy; October 2, 2023
 - World Drug Safety Congress United States, Barbara Hendrickson, Brian Waterhouse, Brian Edwards,
 Preston Burns; October 18, 2023

BRATS: 2024 Objectives

- Continue sharing and learning of visualization tools and strategies to assist benefit risk assessment from members across organizations
- Go Live for the App internal first; experienced folks from companies and/or other experts to provide feedback





Workstream 2 (co-leads: Melvin Munsaka, Judy Li)

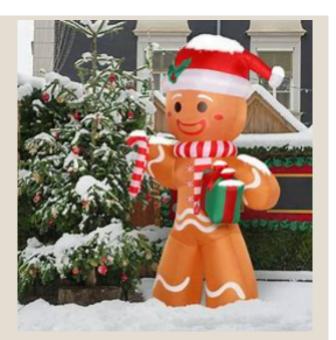
Leadership Team in 2024

Workstream 2 (co-leads: Melvin Munsaka, Judy Li, Michael Fries)

Workstream 2

2023 Presentations:

- At Duke-Industry Statistics Symposium
 - O Special Topics in Multi-Regional Clinical Trial Development
- At DIA/FDA Biostatistics Industry and Regulator Forum
 - Machine Learning and Safety Statistics
- At DIA Annual Meeting
 - The Full Picture: Innovative Software Tools for Data Insight Generation
- At ASA BIOP Regulatory Industry Statistics Workshop
 - Meta-analysis Applications to Safety Evaluation in Clinical Trials
- At Midwest Biopharmaceutical Statistics Workshop
 - O Statistics versus Machine Learning and NLP Approaches Assessment of Drug Induced Liver Injury
- At JSM
 - <u>Leveraging Innovative Methods and Tools for Interactive Quantitative Safety and Benefit-Risk Assessment</u>
- At the Joint NICASA and ICSA Midwest Chapter Fall Meeting
 - O Statistics versus Machine Learning and NLP Approaches Assessment of Drug Induced Liver Injury
- At the Chinese Course of Drug Development and Regulatory Sciences at Peking University
 - The Emerging Landscape on the Use of Machine Learning, Artificial Intelligence, and Natural Language Processing in Drug Safety Analytics



Workstream 2

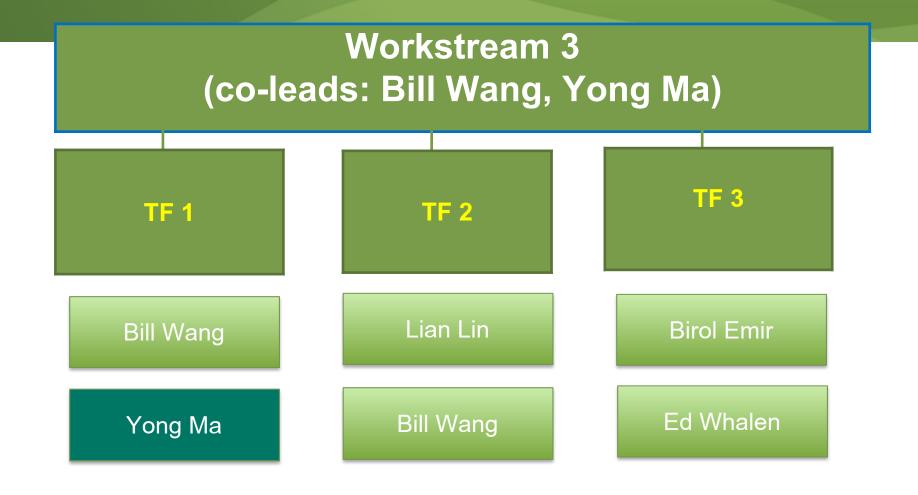
In progress:

- Significant progress on two book chapters for the Deming Workshop Anniversary
 - Considerations in Drug Safety and Benefit Risk in Multi-Regional Clinical Trials
 - Assessment of Spontaneous Reporting Systems: Data Challenges, Analysis Approaches, and Visual Analytics
- Journal of Biopharmaceutical Statistics
 - Submitted manuscript on use of ML, AI, DL, and NLP in drug safety for a special issue of machine learning in healthcare



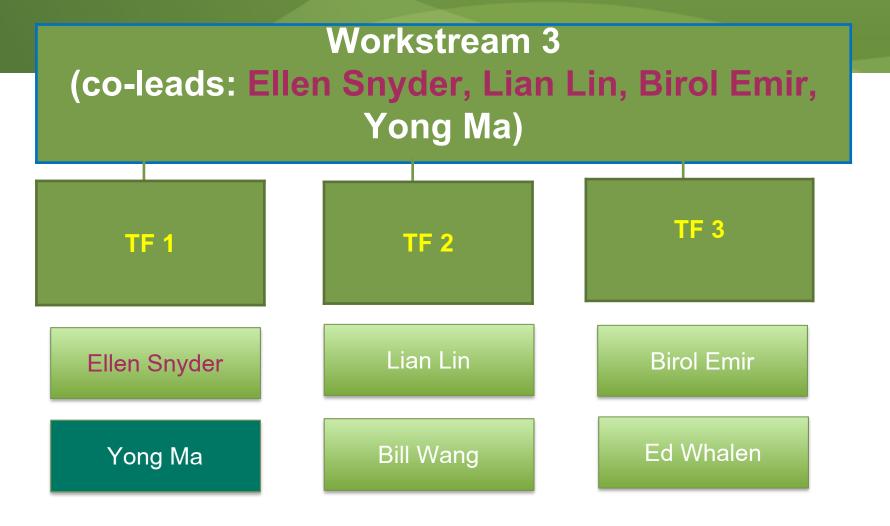


Leadership Team in 2023



Taskforce Non-regulatory lead

FDA scientific lead



Taskforce Non-regulatory lead

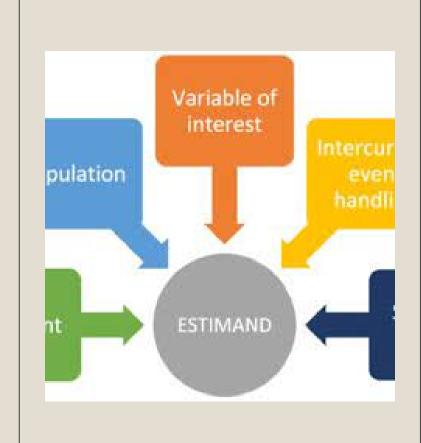
FDA scientific lead

RCT RWE

Workstream 3 Integration of RCT and RWE for Safety Decision Making

Overall accomplishments

- Deep dive on the alignment of estimand framework in RWE & draft manuscript for peer-reviewed journal
- Use case studies to expand into multi-regional context
- Examine the state of the art in RCT-RWE hybrid approaches to causal inference in drug safety
- Presentations
 - Invited session at JSM 2023
 - Roundtable at The ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop



Workstream 3 Integration of RCT and RWE for Safety Decision Making

Taskforce 1: Statistical and design considerations for real world evidence in health decision making

- Completed a focused literature review on estimand framework in the observational safety studies
- Presented at the JSM contributed session "Estimand Framework in Safety Assessments" (August 6, 2023)
- Drafted a manuscript and will submit for a peer-review journal
- Will present at ISBS 2024 invited session Estimands: From randomized clinical trials to non-randomized studies



Workstream 3 Integration of RCT and RWE for Safety Decision Making

Taskforce 2: Design and Analyses of the Pharmacoepi Studies





In drafting the manuscript on multiregional pharmacoepi studies



Established plan to collaborate with WS1 on the background rates for IND safety reporting



Co-organized roundtable discussion in RISW with other WS3 members

Planned 2024 conference presentations:

- ISBS 2024 invited session Considerations for safety analyses when using Real-World Data as external controls to supplement clinical trials
- PV&RM 2024 invited session Use of Real-World Data and Real-World Evidence in Safety

Workstream 3 Integration of RCT and RWE for Safety Decision Making

Taskforce 3: Advanced methods and analytics in application to RCT and RWE

- Developed initial plan and data sources for RCT/RWD case study
- Produced statistical data review examples of safety monitoring in ongoing trials
- Presented statistical data review examples at the 2023 DIA in Boston
- Considerations for rest of 2023:
 - Finalize analysis plan for RCT/RWE hybrid study example
 - Produce draft a manuscript on the RCT/RWE hybrid case study (based on existing data)
- ISBS proposals for 2024 accepted
 - Considerations for safety analyses when using Real-World Data as external controls to supplement clinical trials
- JSM 2024 invited session accepted
 - Toward a Common Framework for Use of Real-World Evidence in Drug Development



Leadership Team in 2023

Outreach and Communication Team (lead: Michelle Zhang)

Scientific Webinar

Mengchun Li

Susan Mayo

General

Michelle Zhang

Non-regulatory lead

FDA scientific lead

Outreach and Communication Team (lead: Michelle Zhang)

Scientific Webinar

Michelle Zhang

Susan Mayo

General

Michelle Zhang

TBD

Non-regulatory lead

FDA scientific lead

Communication and Outreach

Scientific Webinar

- Mar 20, 2023. Signal Detection in Clinical Development--- Leveraging Interactive Safety Graphics (ISG) Tools in the Aggregated Safety Assessment Planning Framework.
 - Presenters: Barbara Hendrickson, Cindy McShea, Boaz Mendzelevski
- Jul 17, 2023. Assessing the Use of the Estimand Framework in Recent Pharmacoepidemiologic Post-market Safety Studies
 - Presenters: Susan Mayo, Ellen Snyder, Yong Ma
 - Panelists: Hana Lee, Jie Chen, Wei Liu
- Oct 2, 2023. CIOMS Working Group (WG) XII Report 2023 10 02 SWG 03 Scientific Webinar YouTube
 - Presenters: Hong Yang, Leo Plouffe
 - Panelists: Lisa Rodriguez, Mike Colopy

Updated webpage at ASA BIOP Section: Safety Working Group

<u>Created YouTube Channel</u> <u>SWG@YouTube</u> in Sep 2023

Actively engaged LinkedIn: <u>SWG@Linkedin</u>

Created working group Email: Safe YouTube mail.com in Sep 2023





