Cardiac Safety Research Consortium Annual Meeting

Future Areas of Focus & Opportunities

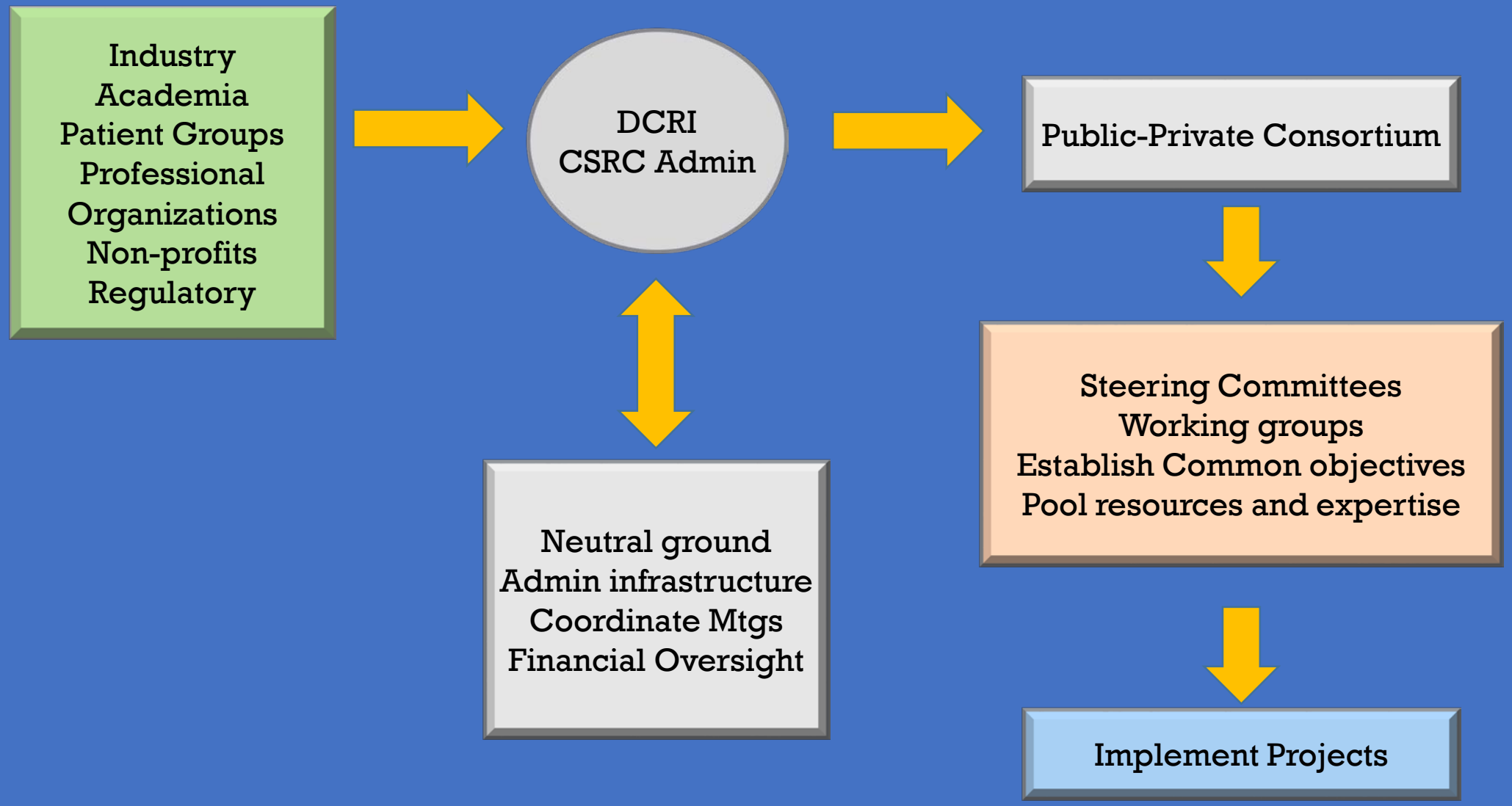
18 October 2016

CSRC MISSION

To advance scientific knowledge on cardiac safety for new and existing medical products by building a collaborative environment based upon the principles of the FDA's Critical Path Initiative as well as other public health priorities

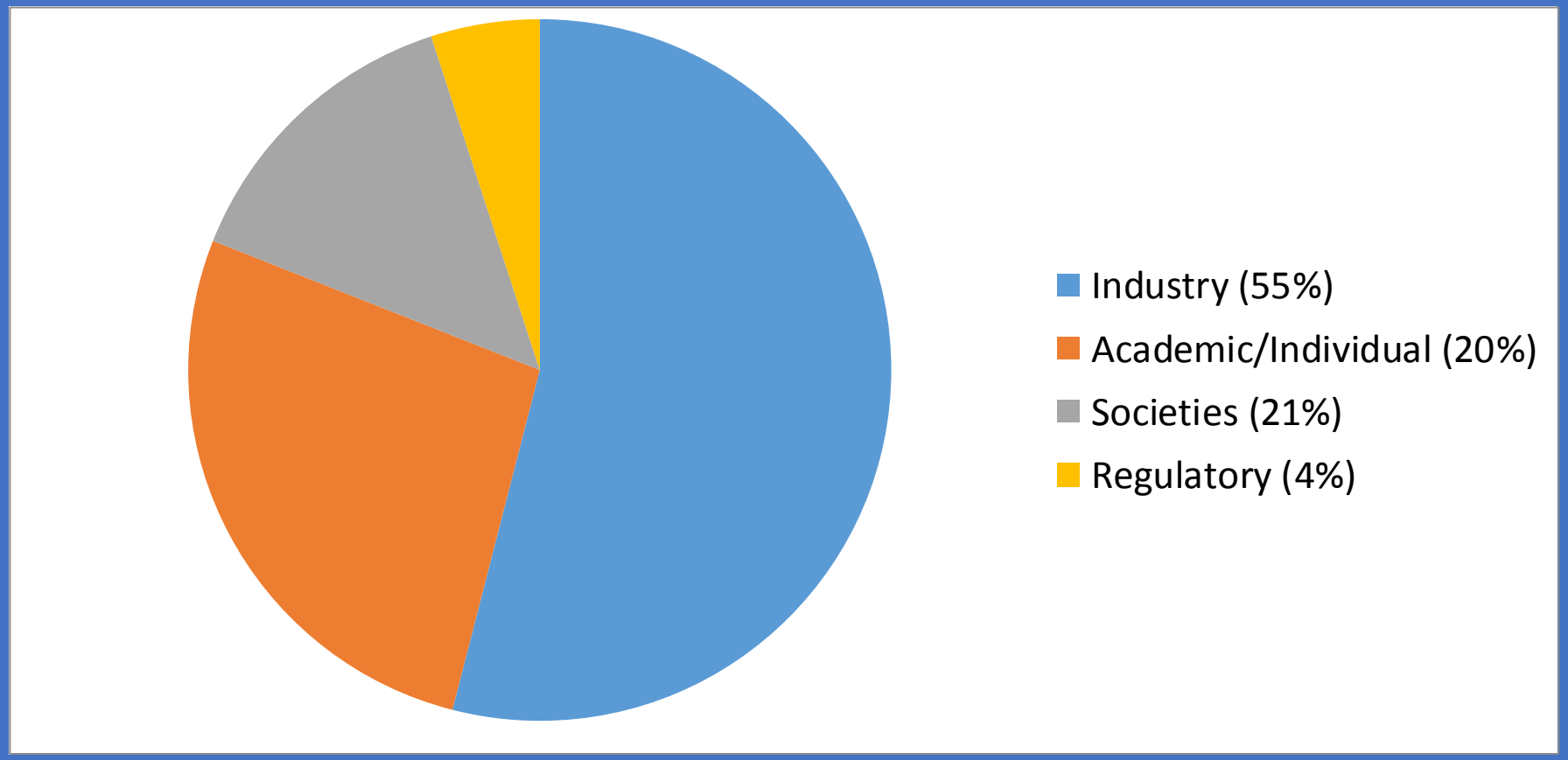
CARDIAC SAFETY RESEARCH CONSORTIUM

CSRC Public-Private Partnership Model



CSRC Organization & Committees

Membership & Collaborations



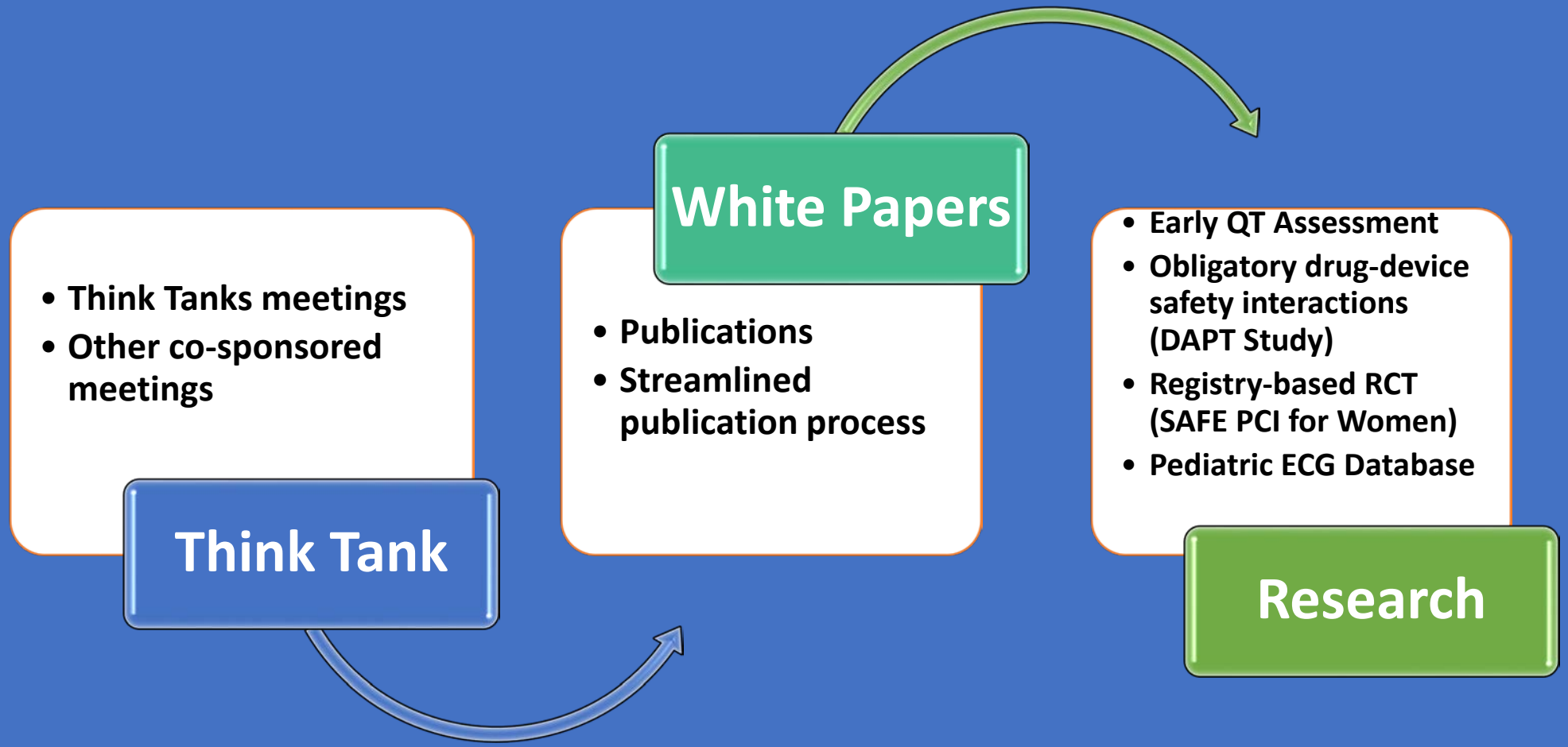
WHAT WE DO

Bring people and groups together to address cardiac safety issues for drugs and devices in all therapeutic areas

Pre-competitive environment – designed so that participation will benefit everyone – goal of improving public safety

Pooling of resources allows us to address issues that we all face but may not be able to solve on an individual basis

HOW WE DO IT


• Think Tanks meetings
• Other co-sponsored meetings
Think Tank
White Papers
• Publications
• Streamlined publication process
• Early QT Assessment
• Obligatory drug-device safety interactions (DAPT Study)
• Registry-based RCT (SAFE PCI for Women)
• Pediatric ECG Database
Research

CSRC SURVEY

- Critically important to receive feedback from our diverse membership in order to enhance and further focus potential or future CSRC research projects and meetings.
- The CSRC aims to focus on drug and device CV safety issues that are relevant to our membership and to create collaborative efforts (meetings, research, education) that are of significant impact and move the science forward.
- The CSRC Survey is an opportune time for CSRC members to contribute to the direction of the educational, meeting, and research missions of the CSRC.

Survey Feedback
Follow-Up -- Think Tanks of Interest

1. Atrial fibrillation and ablation
2. Stem cell therapy and cardiac safety
3. Blood pressure
4. COPD
5. Thorough QT studies & QT Assessments
6. Diabetes
7. CRF Forms for Non-CV Studies
8. CardioOncology
9. Outcomes Studies
10. Reversal Agents and NOAC
11. Pediatrics and Cardiac Safety

Survey Feedback
Future CSRC Think Tanks Proposed

- Drug interactions (patients on multiple drugs with known/suspected QT effects) and QT prolongation
- Detection and prevention of cardiac toxicity in oncology trials
- Review of Beta-blockers; safety/efficacy in different cardiac conditions
- Combined cardiorespiratory function safety assessment
- Antidiabetes and CVOTs
- Critical comparison and evaluation of imaging modalities performance for following changes in LV and RV function in oncology trials
- Transcatheter aortic valve replacement
- CVOTs for non-CV drugs
- Optimal benefit-risk for early phase drug development & assessments to ensure low CV risks
- Atrial fibrillation and heart failure: preserved HF, anemia and CV risk
- Arrest of atherosclerosis – clinical and regulatory approach
- Regenerative medicine beyond stem cells
- Monitoring tools to evaluate induced autonomic effects in drug development

Survey Feedback
New Areas of Research CSRC Should Pursue

- Inventory of drugs with non-QT related cardiac toxicities
- Reasons for the high proportion of atrial fibrillation post artificial valve surgery – is it the valve or surgery?
- CardioOncology / CardioOncology iatrogenic CHF prevention trial
- Cardiac drug-drug interactions with Direct Acting Antivirals (DAA)
- Antidiabetes and cardiac safety
- Optimizing design and analysis of CVOTs for non-CV drugs
- Renal disease and CV outcomes
- Research on emerging cardiac safety concerns
- Biomarkers and ability to predict Phase 3 outcomes
- Clinical use of genomics
- The growing lack of development of novel molecular entities in cardiology
- Translation of the CIPA initiative into the clinic – prospective evaluation of positive and negatives, examples

Survey Feedback
Proposed Research Projects

- CSRC should move beyond white papers and think tanks. Survey studies, collaborations on architectures for EMR-based pragmatic clinical trials and collaborative investigations of novel techniques in drug safety assessment
- Explore safety and efficacy of NOACs in patients with cancer (AF/cancer or VTE/cancer)
- Validation of CIPA initiative with compounds

Survey Feedback
Proposed White Papers

- Quality of life impact of CV treatments
- Development of AF: causes and prevention
- Setting up a biomarker library with validated or need for validated biomarkers for each component of cardiac function
- Follow-up on outcome studies in diabetes
- Biomarkers and CV outcomes
- Role of the FDA in new product development
- Evaluation of autonomic effects in drug development

Survey Feedback
What Can CSRC Do Better?

- Better communication of ongoing projects & dissemination of results of completed projects/papers
- More opportunities to participate in White papers
- Be neutral and not endorse or favour certain members
- These surveys are useful / Be more timely with surveys
- Anxious to see how the CSRC works
- Be more PROACTIVE
- Continue to strengthen regulatory interactions

Survey Feedback
Additional Feedback

- Be more involved in clinical practice – need to know our research makes a difference
- Improve endpoints for CVOTs
- Need to also focus on efficacy not just safety
- Keep up the good work

An Additional Proposal

- Create educational materials on “the science of cardiac safety” to be used in pharmacy, medical, and nursing schools to educate future healthcare practitioners about the safe use of drugs with a certain degree of QT prolongation liability. This would involve two components:
  - 1) Explanations of TQT studies, concentration-exposure modeling, and CiPA, the research studies that lead to labeling information; and
  - 2) Education about clinical risk factors for the actual occurrence of *Torsades*

WANTED: CSRC INVOLVEMENT

There are areas that everyone can find direct benefit/take home for their “day jobs”

Success is dependent upon your participation

- **Participation on a project team**
- **Leading a project**
- **We need your proposals!**

CSRC will provide infrastructure to ensure your project/area of interest successful in a reasonable time frame

CSRC SUCCESS

Everything we do is focused on:

- **Common issues we all face but perhaps cannot address on our own**
- **Practical advice, suggestions, approaches that we can apply in our day to day work as drug/device developers or clinicians**
- **Improving efficiency, effectiveness, overall safety of drugs/devices that ultimately make it to patient use**

Panelists