External Peer Review of the Clinical Immunization Safety Assessment (CISA) Network, Immunization Safety Office, Division of Healthcare Quality Promotion
December 9-10, 2010, Atlanta, Georgia

Executive summary

Panel Charge and Deliberations

The CISA External Program Review was conducted to assess the contribution of this project to public health at CDC's Immunization Safety Office and provide expert guidance to CDC regarding future directions for research into the biological basis of adverse events following immunization (AEFI) and translation of that research into evidence-based clinical strategies for providers. The panelists were asked to consider three questions related to CISA's goals.

Goal 1: To study the pathophysiologic basis of adverse events following immunization
Goal 2: To study individual risk factors associated with developing an adverse event following immunization, including

- identify and characterize genetic risk factors; and
- maintain a bio-specimen repository from people who have experienced adverse events following immunization

Goal 3: To serve as a vaccine safety resource for consultation on complex clinical vaccine safety issues
Goal 4: To assist domestic and global vaccine policy makers in developing strategies to assess individuals who may be at increased risk for AEFI

- Develop evidence-based strategies for evaluating adverse events following immunization
- Develop evidence-based strategies for re-vaccination of individuals who have prior AEFI.

The panelists were asked to consider the following three questions

1. How well do the CISA goals fit with the public health mission of CDC/ISO?
2. For the goals that are appropriate for the CDC/ISO mission, how would you prioritize these goals, and why?
3. What is the best approach to accomplishing these goals?

External Review Panel Comments and Recommendations summary

Several cross-cutting challenges were identified:

- Studies of vaccine adverse reactions can be complex and many pathophysiologic mechanisms of health outcomes are unknown regardless of vaccine exposure
- Studies of genetic bases for AEFI can be particularly difficult due to the high costs and highly technical and rapidly evolving field
- Because of high vaccination coverage among children in the United States, it is challenging to identify unimmunized (comparable) control groups
- It is difficult to identify and recruit large numbers of patients with severe vaccine adverse reactions needed to conduct a well-powered study, due to the rarity of such reactions
- It is difficult to obtain medical records (if a dataset is not already available) and maintain the Health Insurance Portability and Accountability Act (HIPAA) data privacy requirements
- When AEFI cases are identified through reporting to VAERS, it is difficult to obtain biological specimens in a timely manner

Question 1: How well do the CISA goals fit with the public health mission of CDC/ISO?

CDC's mission is to collaborate to create the expertise, information, and tools that people and communities need to protect their health through health promotion, prevention of disease, injury and disability, and preparedness for new health threats (http://www.cdc.gov/about/organization/mission.htm)

The mission of ISO is to assess the safety of vaccines administered to children, adolescents and adults. It is a comprehensive approach to vaccine safety that includes:

- Surveillance to detect possible adverse events following immunization (AEFI) in a timely way
- Investigation and research of possible AEFI to determine causality and risk factors
- Development of strategies for prevention of AEFI
- Timely communication and education to partners and public.

Discussion

In general, the reviewers felt that CISA's goals represent appropriate functions within the public health mission of immunization programs. Not all of CISA's goals fit well with CDC's traditional public health mission; however, the reviewers felt that the CISA

project fills a gap in the study of vaccine safety that is unique. CISA does not have an obvious fit into the mandate of any federal agency. CISA resources are insufficient to accomplish all the goals, particularly goal #1 (pathophysiology).

Recommendations from panel members:

- Modify activities within CISA to be more consistent with the public health mission of CDC.
- CISA activities should be oriented toward public health goals rather than pursuing basic science research on either the pathophysiologic basis of AEs or possible genetic risk factors. Many aspects of basic science are outside the mandate of CDC, and CISA sites are not sufficiently funded to perform basic science research (Goal 1 and Goal 2).

Question 2. For the goals that are appropriate for the CDC/ISO mission, how would you prioritize these goals, and why?

Discussion
Panelists decided to prioritize all CISA goals and agreed that goals should be prioritized in the following order: goals #3 (provide consultation and serve as a vaccine safety resource) and #4 (develop guidance) ranked highest, then #2 (identify individual risk factors), then #1 (pathophysiology).

Recommendation from panel members:

- Goals 3 and 4 should be primary
- A secondary priority is goal 2, followed by goal 1 (perhaps led by other partners)
- Add another goal that focuses on training of future vaccine safety experts

Question 3. What is the best approach to accomplishing these goals?

Discussion
The panelists' comments were requested on the current ISO/CISA approach and the expertise and other resources needed for each, including the possibility of more active involvement or collaboration with other groups (e.g., NIH), and any other suggested approaches. Panel members stated:

- CISA is currently spread too broadly and thinly; pursuing the four goals in a more streamlined manner may be beneficial
- A specimen biorepository capability is valuable but cost-prohibitive for CISA and CDC. Bio-banking is a very complex undertaking requiring unique expertise and resources.

- Explicit evaluation criteria would be valuable in monitoring CISA performance, but currently such criteria do not exist

Recommendations from panel members:

- ISO should determine whether epidemiologic risk factor studies should be done by CISA versus systems accessing large population databases
- Goal #1 (study pathophysiologic basis of AEFI) could be pursued through collaborations with NIH, DoD, FDA, or other groups; or through ad hoc funding from ISO.
- CDC should explore lessons learned from other government programs that evaluate individual patient issues (e.g., OSHA's Pediatric Environmental Health Specialty units (PEHSU), DoD's Vaccine Safety Network with a DNA repository).
- Partnering with other agencies or existing facilities for establishing a bio-specimen repository should be explored by the government.
- CDC should implement evaluation criteria for the remainder of the current contract.
- Future efforts should emphasize goals #3 and #4, providing consultation services and developing guidance for providers.
- CDC should consider focusing projects in fewer sites, providing more direction for researchers, and ensuring that projects are not duplicative of those being conducted through the Vaccine Safety Datalink or other CDC-sponsored projects
- An explicit statement as to how CISA contributes to NVAC's creation of the "ideal vaccine safety net" should be crafted.
- Better integration of these activities with NIH and other Federal agencies is needed.
- Increased communications between ISO and project PIs, including direct communications with VAERS surveillance staff, would enhance CISA efforts.
- CDC should consider alternative funding mechanisms to achieve the most impact from CISA activities.
- Fellowship programs to train future vaccine safety experts should be supported
- CDC should consider utilizing a voluntary committee to provide guidance/management advice to physicians, as is done by WHO/SAGE
- CDC should consider addition of an additional box on the VAERS report form to indicate willingness to participate in research