ENGELBERG CENTER for Health Care Reform at BROOKINGS

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CDER Use of Mini-Sentinel (MS) Tools, Approaches, and Resources in Analyses of Post-Market Drug Safety

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Summary

- Variety of assessment approaches/tools with different capabilities: approaches/tools are not equivalent
- Continuing enhancement of these approaches/tools
- Benefit of these tools, and the MS population, to FDA
- Focus on comparison of two approaches/tools:
  - Modular Programs & Protocol Based Assessments
- Early in the post-marketing period, and in other situations where there is not much exposure data available, it is important to have tools and approaches well suited to this situation
- Select the approach/tool which maximizes usefulness of data available

Safety Issue Assessment

- Concerns from pre-approval studies
- Unexpected potential signals from FAERS or other sources
- Unexpected volume of reports for known potential adverse events
- Examine potential safety signals throughout the post-market life of drugs
  - Newly approved drugs
  - Drugs on the market for some time
  - Drugs with limited use, or assess outcomes in individuals who have been using drugs of interest for a long time, or in individuals with specific use circumstances (e.g. concomitant use, particular co-morbidities, etc.)

Protocol Based Assessments

- Essentially a complete epidemiologic study
- Ability to look at primary, secondary analyses, sensitivity analyses, population subgroups
- Well adjusted estimate of risk
- One time look or sequential repeated analysis

Caveats:

- Lengthy
  - takes time to design, program, execute, and evaluate results
- Not always feasible
  - requires sufficient number of exposed individuals, sufficient power to accomplish goals

Modular Program – exposure/outcomes

- Rapid results since modules are pre-programmed
- Stratification by age, gender, year
- Produce incidence rates for currently exposed population
- Can provide information regarding whether or not a large increased risk may exist
- Can provide additional evidence for safety issues identified from other data sources

Caveats:

- Limitations in outcome definitions, criteria for eligibility and exclusion
- No adjustment for confounders, no estimate of risk

Modular Program Utilization

- Rapid look at the events of interest in exposed population and a comparison population
- Obtain some data in cases of a high level of concern about determining if a potentially serious public health issue exists
- May not have power (sample size / level of uptake / exposure) to benefit from a protocol based assessment
  - While adjustment for confounding is ideal there may not be enough exposure to do this
- Complete epidemiologic study will take some time to deliver results

Modular Program ≠ Protocol Based Assessment

- Results of a modular program do not substitute for results of a protocol based assessment

- Implementing a modular program to address a question may be done even if the intent is to perform a protocol based assessment when exposure is sufficient

Modular Programs

- Limitations in outcome algorithms
- Limitations in eligibility/exclusions
- No adjustment for confounding
- Rapid turnaround from specifications to results
- No de novo programming required
- One time analysis
- Results provide an idea of levels of adverse events
- Valuable to provide a level of assurance or indication as to whether or not a large increased incidence of adverse events exists
- Provide information that supports results from other data streams

Protocol Based Assessments

- Complex outcome definitions
- Complex eligibility/exclusions
- Adjustment for confounding assuming sufficient exposure
- Requires significantly more time
- Sequential or one time analysis
- Requires de novo programming
- Results provide adjusted estimates of risk
- Allows for complex analyses

Modular Programs

- Limitations in outcome algorithms, eligibility and exclusion criteria
- No adjustment for confounding
- Rapid turnaround from specifications to results
- No de novo programming required
- One time analysis
- Valuable to provide a level of assurance or indication of potential signal for adverse events

PROMPT*

- Semi-automated
- Adjustment for confounding
- Sequential or one time analysis
- Preprogrammed design and statistical options

Protocol Based Assessments

- Complex outcome definitions
- Complex eligibility/exclusions
- Adjustment for confounding assuming sufficient exposure
- Requires significantly more time
- Sequential or one time analysis
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*Prospective Routine Observational Monitoring Program Tools

Thank You,

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