Summary of Results from Pregnancy Testing in Clinical Trials Survey
Survey on Pregnancy Testing Protocols

- CTTI targeted stakeholders involved in the design, conduct, and evaluation of clinical trials
- Invited 58 individuals and received 35 completed surveys, 4 partially completed
- Web-based survey with questions regarding experience and opinions on appropriate pregnancy testing protocols in five clinical study scenarios
Purpose of Survey

- Factors going into decision making about pregnancy testing
- Variability in
  - What decisions were made
  - What factors influenced decisions
- To inform discussion at this meeting, NOT to draw general inferences about the state of pregnancy testing in the research community!
Response Status

- **Academia**: 25
  - No response, n=21
  - Partially Completed, n=1
  - Completed, n=3

- **CRO**: 5
- **Government**: 3
- **Industry**: 20
  - No response, n=18
  - Partially Completed, n=1
  - Completed, n=1
- **IRB**: 1
- **Research Sites**: 1
  - No response, n=1
  - Partially Completed, n=1
  - Completed, n=1

May 20, 2011

CDER - Office of Medical Policy
Selected Data from Responses to Survey
Which best describes your organization?
Please check all that apply*

- Academic Medical Center
- Non-academic Clinical Research Site
- Clinical Research Organization
- Institutional Review Board
- Industry
- Government (FDA, NIH, VA)
- Other

*42 responses. More than one response allowed, partial surveys included.
Which do you consider your PRIMARY area of clinical experience/expertise?

- Women's health/obstetrics & gynecology
- Internal medicine (including subspecialties)
- Neurology/psychiatry
- Nursing
- Pharmacology or pharmacy
- Other
### Survey Scenarios

<table>
<thead>
<tr>
<th>Scenario</th>
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<tbody>
<tr>
<td><strong>Phase III study</strong> - new analog of thalidomide - administered for 12 months - assume two methods of highly effective contraception</td>
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<tr>
<td><strong>Phase III</strong> - new indication for a currently marketed drug - administered for 6 months - currently classified as Pregnancy Category C - assume subjects using highly effective method of contraception.</td>
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<tr>
<td><strong>Phase II study</strong> - new intravenous antiemetic for prevention of postoperative nausea and vomiting (PONV) - exposure limited to the perioperative period - drug elimination half-life is 6 hours - and preclinical studies show no signs of reproductive toxicity - assume subjects are using a highly effective method of contraception.</td>
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<tr>
<td><strong>Phase I study</strong> - new chemotherapeutic agent - advanced cancer patient population - the agent is administered once weekly for 4 weeks - assume subjects are using a highly effective method of contraception.</td>
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<tr>
<td><strong>Phase II study of a new chemical entity (NCE)</strong> - with no worrisome preclinical data on reproductive toxicity - administered for 6 months - assume subjects are using a highly effective method of contraception.</td>
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Survey Scenarios

- Varied in degree of
  - Risk to embryo/fetus
  - Certainty about risk to embryo/fetus
  - Implicit risk of pregnancy
    - Condition
    - Duration of study

- Not much detail (on purpose!)
- Interested in how responses varied across risk
- Interested in free text responses
Would you recommend excluding pregnant women from this study?

Percentage of Respondents Who Answered “Yes”

- Ph III Thalidomide Derivative: 100%
- Ph III Cat C New Indication: 90%
- Ph II Antiemetic PONV: 70%
- Ph I Chemo Adv CA: 85%
- Ph II NCE: 90%

Ph I Chemo Adv CA
Ph II NCE
What is the acceptable risk of a false negative pregnancy test?

Percentage Choosing .001% or .01% Risk of False Negative
What is the acceptable risk of a false negative pregnancy test?

Percent Choosing Each Level of Acceptable Risk of False Negative

Ph III Thalidomide Derivative
Ph III Cat C New Indication
Ph II Antiemetic PONV
Ph I Chemo Adv CA
Ph II NCE

0.001
0.01
0.1
1
Relative Importance of NPV, Patient Burden, Researcher Burden, Cost

Average Importance Rating of NPV

- Ph III Thalidomide Derivative: 4.5
- Ph III Cat C New Indication: 4.0
- Ph II Antiemetic PONV: 3.5
- Ph I Chemo Adv CA: 5.0
- Ph II NCE: 4.5
Relative Importance of NPV, Patient Burden, Researcher Burden, Cost

Ph III Thalidomide Derivative
Ph III Cat C New Indication
Ph II Antiemetic PONV
Ph I Chemo Adv CA
Ph II NCE

- NPV
- Subject burden
- Study burden
- Testing costs
Consistency!

Recommend Exclusion

- Ph III Thalidomide Derivative
- Ph III Cat C New Indication
- Ph II Antiemetic PONV
- Ph I Chemo Adv CA
- Ph II NCE

Graph showing NPV, Subject burden, Study burden, and Testing costs.
Type of Test

Test Type

- Home test by patient
- Point of care urine by study staff
- Urine by lab
- Serum by lab
Timing of Test

Percentage Choosing Testing Whenever Convenient for Subject

- Ph III Thalidomide Derivative
- Ph III Cat C New Indication
- Ph II Antiemetic PONV
- Ph I Chemo Adv CA
- Ph II NCE
Timing of Test

Recommend Exclusion

Percentage Choosing Testing Whenever Convenient for Subject
What Study Time Points for Testing?

- Ph III Thalidomide Derivative
- Ph III Cat C New Indication
- Ph II Antiemetic PONV
- Ph I Chemo Adv CA
- Ph II NCE

- Before, during and after
- Before and during
- Before only
Timing Relative to Study Drug

- Ph III Thalidomide Derivative
- Ph III Cat C New Indication
- Ph II Antiemetic PONV
- Ph I Chemo Adv CA
- Ph II NCE

- At screening and prior to drug admin
- Prior to drug admin
- At screening
Frequency of Testing

Percentage Choosing to Test Every Month During Study

- Ph III Thalidomide Derivative
- Ph III Cat C New Indication
- Ph II Antiemetic PONV
- Ph I Chemo Adv CA
- Ph II NCE
Frequency: Other Responses

- Per protocol
- Missed menses
- Subject missed contraception
- More frequently during first trimester
- Same interval as study visits
- Depends on effectiveness of contraceptive method
How long after study would you follow-up with pregnancy testing?

- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%
- 100%

Ph III Thalidomide Derivative
Ph III Cat C New Indication
Ph II Antiemetic PONV
Ph I Chemo Adv CA
Ph II NCE
Other Issues/Feedback

- Ambiguity about effectiveness of contraception
- Ambiguity about drug metabolism relative to follow-up question
- Ambiguity about timing of testing--should have included “prior to study drug administration”
- Ambiguity about age of subjects
- ?Female partner of male patient taking drug?
General Impressions

- NPV most important
  - Responses to other questions mostly consistent with that
- Factors affecting NPV (age, contraceptive method, type and timing of test) considered, but some variability
Discussion