

Implications for Pediatric Research

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Importance of inclusion of children

- Benefit from advances in science
- New therapeutic agents
- Pediatric indications of per-existing drugs
- Safety and efficacy of agents accurately and prospectively determined

Alternatives are not acceptable

- Excluding or limiting access to clinical drug trials → limited therapeutic advances for children's conditions
- “Testing” agents outside of clinical drug trials in practice settings with uncontrolled monitoring

AAP support of initiatives to promote participation of children

- NIH guidelines on inclusion of children
- Best Pharmaceuticals for Children Act
- Pediatric Research Equity Act

Imperfections in clinical drug approvals and safety monitoring

- Inherent conflicts of interest in private for-profit business developing therapeutic agents to advance public good
- Direct marketing with insufficient information by which public can determine benefits and risks

Restrict clinical trial database to clinical DRUG trials

- Clinical drugs already overseen by FDA
- May include biologics and medical devices in initial registry
- Then expansion (or establishment of alternative databases) to include other forms of clinical trials

Potential of registry to increase accountability and communication

- Goal is to rapidly disseminate important and accurate information
- Getting *mis*information quickly is worse than getting accurate information after time delay
- Ready availability of information should be weighed against risk of disseminating inaccurate or misleading information

Registry should bolster, not undermine, peer review process

- Peer review process: research findings from small number of individuals (may have inherent bias or conflict of interest) becomes vetted by larger group
- Peer review may be associated with barriers to rapid distribution of knowledge
 - Many addressed through technology
 - Some residual delays unavoidable given care required by thoughtful review

Benefits of full disclosure

- Even if delayed, will establish accountability for clinical drug trials
- Trials that have shown lack of efficacy will be available for review → will reduce unsubstantiated claims of drug efficacy
- Registry should be used for new indications or formulations of already approved products → will allow pediatricians to identify when drugs have been shown ineffective for children

Need to ensure information is accurate

- Must be mechanisms for:
 - Review of findings before posting
 - Correction of misleading, inaccurate or outdated information
 - Active monitoring and quality checks
 - Penalties for knowingly posting misleading or inaccurate information
- Providing drug company results to public without peer review = advertising

Presentation of clinical drug trial results

- Present findings in a manner comprehensible to general public
- Important key findings and information of value to clinician/researcher are not lost
- Rendering scientific information comprehensible to public not easy task; even medical community has difficulties interpreting some scientific findings

Will registry accelerate access to information by physicians?

- Drug companies have incentive to provide information to clinicians as early as possible about newly approved drugs and indications and have the means to do so
- Unlikely that registry will accelerate this process
- Proposed legislation: unsubstantiated data can appear quickly; substantiated and critical data will be delayed

Problem with lack of peer review prior to posting on website

- Individuals and companies may make claims of efficacy based on “research findings” that would not be judged adequate if subjected to peer review
- Question: whether these findings will be posted, even if noted to be “preliminary”?
- False information could result in harm
- An attitude of “buyer beware” is not appropriate for healthcare treatment decisions

Potential immediate impact of registry

- Opportunity to query database for pediatric indications of already approved drugs
- Pediatricians may be posed with numerous questions about planned, ongoing, or very recently completed studies
- Direct advertising has been shown to influence drug prescribing in negative ways
- Registry would provide far more information, potentially **prior** to FDA approval and peer review

Is this an efficiency we should be striving to achieve?

- Posting of non-reviewed clinical drug trial data, coupled with direct advertising and ability to obtain drugs over the internet without a prescription → medication can go rapidly from design to use by public without ANY competent medical advice or oversight

Support for clinical trial registry?

- Not a question of whether or not we should support clinical trial registries, but rather how it would best be done
- Bring together constituencies with goal of designing and implementing registry initially focusing on clinical drug trials and medical devices
- Models of well designed registries, such as clinicaltrials.gov, should be used as starting point

Should registry serve as access point to enter trials?

- May be possible in select cases, such as trials for serious conditions and/or trials conducted on NIH campus
- In most situations it is not feasible
 - Open national enrollment does not permit close monitoring of subjects
 - Most projects do not have resources to enroll at national level

Will requirements dissuade researchers?

- Drug companies have more resources to comply with requirements than would independent or practice-based researchers
- Will be critical that reporting requirements are not overly burdensome so that they become disincentive to conducting clinical drug trials by other qualified researchers (these researchers may have less conflicts of interest)

Monitoring research to ensure no omissions on registry

- How will omissions be detected?
- How will we know that all clinical drug trials have been entered?