Clinical Trial Disclosures

.....roadmap for a moving target
Disclosure

* EITHER
* I have no relevant financial relationship in relation to this educational activity
* OR
* I have relevant financial relationship(s) with respect to this educational activity with the
Clinical Trial Disclosures

- Background
- Compliance
- Business Model
- Technology
- Workflow Steps
- International Registries
Background

- What are trial disclosures?
Background: Data
Background: Benefits

- Greater efficiency by reducing unnecessary **duplication** of research effort
- Potential for higher **recruitment** rates of clinical trial participants
- Better accountability and compliance of **results**
- Unbiased **source** of information about trials
- Improving available **evidence** to inform treatment practice and health care
Food and Drug Administration Amendment Act (FDAAA) of 2007 requirements:

- "Applicable Clinical Trials"
  - Initiated after 9/27/07, or on or before 9/27/07 if ongoing as of 12/26/07
  - Interventional
  - Controlled
  - Phase 2-4
  - FDA Regulated Drug (IND study, site in US, drug manufactured in US)
Compliance: Enforcement

Consequences of Non-Compliance

- Public notices of noncompliance
- Withholding of NIH funds
- FDA sanctions
- Civil monetary penalties (up to $10,000/day)
Authors deemed trials were subject to FDAAA if they were:
- Interventional trials of a drug, device, or biological agent
- Had at least one US site
- Registered as phase II or later

Authors deemed results overdue for a trial if:
- Investigated a drug that already had approval from the FDA
- > 1 year elapsed from trial completion date
- Results were not available on ClinicalTrials.gov

<table>
<thead>
<tr>
<th>Number of ClinicalTrials.gov Records in Prayle Dataset By Type</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventional Trials</td>
<td>83,579</td>
</tr>
<tr>
<td>With Recruitment Status of “Completed”</td>
<td>31,556</td>
</tr>
<tr>
<td>With Completion Date 01 Jan – 31 Dec 2009</td>
<td>5,642</td>
</tr>
<tr>
<td>Deemed “Covered by the FDAAA”</td>
<td>1,465</td>
</tr>
<tr>
<td>Studying an FDA-approved drug (per Drugs@FDA)</td>
<td>738</td>
</tr>
<tr>
<td>Results Not Reported</td>
<td>575 (78%)</td>
</tr>
</tbody>
</table>
Representative Limitations of Prayle Analysis

Did not account for all elements of statutory definition for “applicable clinical trial” of a drug, e.g.

- Controlled
- Clinical Investigation as defined by 21 CFR 312.3

May have included unapproved products

- Manufacturer A has approval for Drug X
- Manufacturer B has approval for Drug Y
- Applicant C is seeking approval for a fixed-dose combination of Drugs X and Y
- FDA would generally consider the fixed-dose combination to be a new drug.

Results may have been timely submitted but were in quality review by NLM prior to posting
FDA Preliminary Review of Prayle Results

<table>
<thead>
<tr>
<th>Source</th>
<th>Results Posted</th>
<th>Results Submitted but in Quality Review</th>
<th>Results Not Required and Not Submitted</th>
<th>Results Appear Overdue</th>
<th>Trial Evaluating Device not Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prayle et al</td>
<td>22.10%</td>
<td>Did not assess</td>
<td>Did not fully assess</td>
<td>77.90%</td>
<td>None noted</td>
</tr>
<tr>
<td>FDA Review: Results Not Submitted (As of Prayle Data Pull in January 2011)</td>
<td>22.10%</td>
<td>6.40%</td>
<td>36.60%</td>
<td>34.60%</td>
<td>None noted</td>
</tr>
<tr>
<td>FDA Review: Results as of 31 May 2012</td>
<td>45.50%</td>
<td>4.90%</td>
<td>31.00%</td>
<td>21.10%</td>
<td>0.40%</td>
</tr>
</tbody>
</table>
Compliance: Enforcement

Enforcement Status

- No fines assessed – yet
- No “wall of shame” posted – yet
- BUT Clinicaltrials.gov does identify studies which haven’t been updated in two years or more

- FDA IS checking for compliance when it does
  Investigations for other reasons
- Enforcement to begin with rulemaking (NPRM)

*We are confident that, when the regulations are in place, the clinical research community will be equipped to comply with the requirements, and the FDA will be able to enforce them more fully. FDA to Henry Wasman & Edward Markey from Director of NIH (Francis Collins)*
Business Model:
De-Centralized vs. Centralized

- Study Team -
  - Clinical
  - Clinical Operations
  - Regulatory & Legal
  - Medical Writing/Stats

- Central Disclosure Team -
  - Workflow Lead
  - Summary Writers
  - QC Analysts

Monthly Updates
For TECHNOLOGY information please contact:

**MMS Holdings Inc.**

**Joe Archer** (Associate Director of Trial Disclosure Services)

6880 Commerce Blvd., Canton MI 48187

Direct Telephone: (734) 738-5111    Fax: (734) 245-0320

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Workflow Steps

For WORKFLOW STEPS information please contact:

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Background: Mandatory International Registries

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<thead>
<tr>
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<th>Registry Name</th>
<th>Study Type</th>
<th>Date</th>
<th>Additional Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Union</td>
<td>EudraCT/EU Clinical Trials Register (EU-CTR)</td>
<td>Phase 2-4 Interventional</td>
<td>Initiated after May 1, 2004</td>
<td>2 site in EEC, or any country if part of a PIP</td>
</tr>
</tbody>
</table>

Welcome to EudraCT

EudraCT is a database of all clinical trials which commenced in the Community from 1 May 2004, and also includes clinical trials linked to European paediatric drug development.

The following tasks can be performed from this page:

Create a EudraCT number

Before any functionality of EudraCT can be used for a given clinical trial, a EudraCT number must be created in order to provide a unique reference for that trial.

Protocol-related information

Sponsors can:
- Create, save XML/PDF files of clinical trial applications locally.
- Load locally saved clinical trial applications to complete, validate, compare, or to prepare a package for submission to a National Competent Authority.

PIP addressees can:
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<tbody>
<tr>
<td>European Union</td>
<td>EU PAS (EU post-authorisation safety studies)</td>
<td>Non-interventional post-authorisation safety surveillance studies</td>
<td>Initiated after July 2, 2012</td>
<td>Imposed as an obligation by a competent authority (EMA)</td>
</tr>
</tbody>
</table>

Electronic Register of Studies

The E-Register of Studies aims to provide a publicly accessible resource for the registration of pharmacoepidemiological and pharmacovigilance studies. Its purpose is to:

- Increase transparency
- Reduce publication bias
- Promote information exchange
- Facilitate collaborations within the scientific community.
- Facilitate optimal use of pharmacoepidemiology and pharmacovigilance expertise in Europe by preventing unnecessary duplication of research.

Registration of studies in the E-Register is mandatory only for "ENCePP Seal Studies"; it is voluntary for all other studies.

If you want to search for studies registered in the database, please click on the button below:

Search register of studies

If you would like to register a new study please click on the button below:

Add Study
### Background: Mandatory International Registries

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<tr>
<td>Argentina</td>
<td>National Register of Health Research (RENiS) - written in Spanish</td>
<td>Interventional trials</td>
<td>Initiated after September 1, 2012</td>
<td>All studies approved by regulatory authority (ANMAT)</td>
</tr>
</tbody>
</table>

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**Curso sobre profesionales y colegios de matriculación en San Luis**

24 de abril de 2014

En la Universidad de La Punta de la provincia de San Luis hoy tuvo lugar la actividad de capacitación orientada a los operadores de Colegios. Participaron referentes de Colegios de Matriculación de San Juan, Mendoza y San Luis.

La apertura del evento, donde se presentaron los ejes de trabajo, estuvo a cargo de Mariana Soratti, responsable del SISA, Cecilia Santa María y Silvina Aranovich, ambas de la Dirección Nacional de Regulación Sanitaria y Calidad en Servicios de Salud que está a cargo del la Red Federal de Registros de Profesionales de la Salud (REFEPS).

Durante la jornada, los referentes provinciales trabajaron en la práctica en el sistema con el alta de profesionales y la gestión colegiada de las matrículas. Asimismo, ejercitaron otras funcionalidades generales de la aplicación.
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**Background: Mandatory International Registries**

### SIIASA

- **Bienvenido!**
  - **Descripción del sistema**: Información de la web portal de SIIASA.
  - **Inicio de sesión**: Iniciar sesión aquí.
  - **Noticias**: Curso sobre profesionales y colegios de matriculación en San Luis.
  - **Notificaciones**: Despachos de documentos y ayuda y documentación de:
    - Argentina en Línea: Formación de personal y capacitación.
    - Agenda Sanitaria: Actualización de establecimientos profesionales y recursos de la red.
    - Central de Reportes: Acceso para generar reportes y estadísticas.
    - Biblioteca: Descarga de documentos de la SIIASA.
    - Acera del SIIASA: Información del sistema, soporte y documentación de:
      - Soporte SIIASA
      - Examen único y otros exámenes de Postgrados.

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<tbody>
<tr>
<td>Brazil</td>
<td>Brazilian Registry of Clinical Trials (ReBEC)</td>
<td>Phase I-IV Interventional</td>
<td>Mandate registration from 27 June 2012</td>
<td>Sites in Brazil</td>
</tr>
</tbody>
</table>

Change ANVISA Resolution Requires Registration Presentation at ReBEC

RDC RESOLUTION # 36 OF 27 JUNE 2012

Changes the RDC No. 30, June 5, 2008, and other provisions...

The Board of the National Health Surveillance Agency, in exercise of the powers conferred upon him by art. 11, item IV of Regulation approved by Decree No. 3029 of April 16, 1999, and in view of the provisions of section II and in § 1 and 3 of article 54 of the Bylaws approved in accordance with Annex I of Ordinance No. 354 of ANVISA, of August 11, 2005, republished in the Official Gazette of August 21, 2006, at a meeting held on June 26, 2012, adopted the following resolution Board and I, the Chairman, determine its publication:

Include art. 1 § 3 and 4 in Article I of the RDC No. 39, June 5, 2008:

"Article 8 ......................"
<table>
<thead>
<tr>
<th>Country</th>
<th>Registry Name</th>
<th>Status</th>
</tr>
</thead>
</table>
| China   | Chinese Public Platform Registry | Intermittent  

Background: Mandatory International Registries (China)

9/15/2014
Clinical trials hold enormous potential for benefiting patients, improving therapeutic regimens and ensuring advancement in medical practice that is evidence based. Unfortunately, the data and reports of various trials are often difficult to find and in some cases do not even exist as many trials abandoned or are not published due to “negative” or equivocal results. However, this tendency for availability of only selective information from the myriad clinical trials conducted is not commensurate with the practice of “evidence-based medicine”. Today, world over, a need has been felt on the imperative for transparency, accountability and accessibility in order to re-establish public trust in clinical trial data. And this would be feasible only if all clinical trials conducted are registered in a centralized clinical trials registry. Registration of trials will ensure transparency, accountability and accessibility of clinical trials.

[Read more...]
**Background: Mandatory International Registries**

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<tbody>
<tr>
<td>Malaysia</td>
<td>National Medical Research Register (NMRR)</td>
<td>All research trials</td>
<td>Beginning in 2006</td>
<td>Conduction in Ministry of Health facilities or funded by MOH grants. Prior ethics review and approval by MOH Research Ethics (MREC)</td>
</tr>
</tbody>
</table>
# Background: Mandatory International Registries

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<tbody>
<tr>
<td>Mexico</td>
<td>NATIONAL REGISTRY OF CLINICAL TRIALS (RNEC)</td>
<td>All research trials</td>
<td>Beginning in Jan 1, 2013</td>
<td>Registration is pre-requisite by regulatory authority (Cofepris) within protocol approval process</td>
</tr>
</tbody>
</table>

[Image of the RNEC website]
### Background: Mandatory International Registries

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<tbody>
<tr>
<td>Philippines</td>
<td>Philippine Health Research Registry</td>
<td>All research trials</td>
<td>Ongoing on or after July 2012</td>
<td>Sites in Philippines</td>
</tr>
</tbody>
</table>

**Philippine Health Research Registry**

The Philippine Health Research Registry (PHRR) is a publicly accessible database of all health researches and clinical trials being conducted in the country.

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Best viewed in Firefox 4+
Background: Mandatory International Registries

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<td>Sites in Philippines</td>
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Background: Mandatory International Registries

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<th>Date</th>
<th>Additional Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>Spanish Clinical Trials Register &quot;REec&quot;</td>
<td>All research trials except Phase 1</td>
<td>Initiated after January 1, 2013</td>
<td>Approved by regulatory authority (AEMPS)</td>
</tr>
</tbody>
</table>
Background: Mandatory International Registries

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<th>Study Type</th>
<th>Date</th>
<th>Additional Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switzerland</td>
<td>Swiss National Clinical Trial Portal (SNCTP)</td>
<td>Phase I-IV Interventional</td>
<td>Initiated after January 1, 2014</td>
<td>Sites in Switzerland. Approved by Regulatory Authority</td>
</tr>
</tbody>
</table>
Background: Mandatory
International Registries

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<tr>
<th>Country</th>
<th>Registry Name</th>
<th>Study Type</th>
<th>Date</th>
<th>Additional Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taiwan</td>
<td>Taiwan Clinical Trials Network</td>
<td>Interventional trials</td>
<td>Initiated after February 27, 2008</td>
<td>Approved by regulatory authority (TFDA)</td>
</tr>
</tbody>
</table>
Thank You

MMS has the people, process and system to manage part or all of your Disclosure Reporting

For additional information or questions regarding Disclosure Services please contact:

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