This is an Executive Summary of a full report prepared by SEC Associates, Inc. Therefore, this Executive Summary does not contain all of the details or information related to the audit.

The audit results set forth in this Executive Summary are subject to all limitations of time and scope set forth herein and are not to be relied upon as an expression of an opinion on (i) overall compliance with laws and regulations or any government or other external standards, (ii) the safety and/or efficacy of the drugs that were the subjects of the trial results audited, (iii) the accuracy or completeness of the clinical trial information provided by Eli Lilly & Company, or (iv) the internal controls and processes of Eli Lilly & Company.
# TABLE OF CONTENTS

I. **INTRODUCTION** .......................................................................................................................... 3

II. **AUDIT OVERVIEW** .................................................................................................................. 4
   A. **APPLICABILITY** ..................................................................................................................... 5
   B. **TIMELINESS** ......................................................................................................................... 5
   C. **ACCURACY AND COMPLETENESS** ..................................................................................... 5
   D. **OUT OF SCOPE** ..................................................................................................................... 5

III. **AUDIT RESULTS OVERVIEW** ................................................................................................ 6
   A. **GENERAL OVERVIEW** ......................................................................................................... 6
   B. **INITIATED TRIALS SUMMARY** .......................................................................................... 7
   C. **CLINICAL TRIAL RESULTS AUDIT SUMMARY** ................................................................. 10
   D. **CLINICAL TRIAL RESULTS (RETROSPECTIVE) AUDIT SUMMARY** .................................. 12

IV. **APPENDIX 1 – LILLY PUBLIC STATEMENT** ........................................................................ 14

V. **APPENDIX 2 – DEFINITIONS, ACRONYMS, AND REFERENCE DOCUMENTATION** ............ 15

VI. **APPENDIX 3 – AUDIT FLOW CHARTS** ................................................................................ 18
   A. **INITIATED TRIALS** ............................................................................................................... 18
   B. **TRIAL RESULTS** ................................................................................................................... 19
   C. **TRIAL RESULTS (RETROSPECTIVE)** ................................................................................. 20

VII. **APPENDIX 4 – AUDIT ASSUMPTIONS, CLARIFICATIONS, AND CONDITIONS** ................ 21
   A. **INITIATED TRIALS (NEW AND ONGOING)** ..................................................................... 21
   B. **CLINICAL TRIAL RESULTS AND CLINICAL TRIAL RESULTS (RETROSPECTIVE)** ............ 23

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June 22, 2006
I. INTRODUCTION

In 1997, the US Food and Drug Administration (FDA) established the requirement for pharmaceutical companies to publicly disclose clinical trials for drugs used to treat serious or life-threatening diseases or conditions (Section 113 of the Food and Drug Administration Modernization Act (FDAMA)). Through a series of events in 2004 and early 2005, numerous organizations\(^1\) and pharmaceutical industry associations\(^2\) became increasingly aware of the public health benefits associated with making more clinical trial information available to the public. As such, the industry made a commitment to freely disclose (on publicly available web sites) clinical trial information for trials registered at initiation and the results of industry-sponsored clinical trials.\(^3\)

As part of this effort, Eli Lilly and Company (Lilly) launched www.LillyTrials.com on December 8, 2004 to demonstrate their commitment to provide enhanced patient care and restore public trust by ensuring accountability and transparency of clinical trial results for Lilly-sponsored trials. This commitment is documented in the Lilly public statement, “Principles of Medical Research Clinical Trial Registry”, dated September 2005 (see Appendix 1). Recognizing the public’s skepticism toward the pharmaceutical industry in general, Lilly set out to demonstrate that its commitment was genuine by allowing an independent third party to review their clinical trial registry process, audit the associated clinical trial information, and to publicly disclose the audit findings.

SEC Associates, Inc. (SEC) performed the independent third party audit of the Clinical Trial Registries (CTRs) www.LillyTrials.com, www.ClinicalTrials.gov, and www.ClinicalStudyResults.org in order to verify adherence by Lilly to its company standards of disclosure (as defined in the Lilly public statement in Appendix 1). Currently, clinical trial registry guidelines are fluid and continue to evolve. Lilly is constantly evolving with the changing industry. In order to avoid auditing a “moving target”, the audit focused on evaluating the CTRs against the requirements defined in Lilly’s September 2005 public statement.\(^4\) In January of 2006, SEC met with Lilly representatives to gain a general understanding of Lilly’s CTR process and procedures for posting clinical trial information. Subsequently, a Clinical Trial Registry Audit Scope and Approach document was created to formalize the scope of the audit, and to obtain agreement regarding the audit process and the source documentation that would be used as the

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\(^1\) The referenced organizations include the American Medical Association (AMA), the World Health Organization (WHO), the International Committee of Medical Journal Editors (ICMJE), and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

\(^2\) Pharmaceutical industry associations include the European Federation of Pharmaceutical Industries and Associations (EFPIA), the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), the Japanese Pharmaceutical Manufacturers Association (JPMA), and the Pharmaceutical Research and Manufacturers of America (PhRMA).

\(^3\) Note that this is a general statement for purposes of providing background information. The exact scope of trials to be included and the information to be included for each trial is described extensively in numerous industry and association documents. Also note that the industry has committed to disclosure of all hypothesis-testing clinical trials, or all clinical trials other than exploratory trials.

\(^4\) SEC did not evaluate the internal controls and processes by which Lilly’s clinical trial information was transferred from their internal records to the three CTR web sites.
A basis against which the CTR web site content would be evaluated\(^5\). After the scope and approach document was finalized, a detailed, on-site audit was conducted by SEC. The on-site audit was followed by remote auditing, discussion of initial findings, review of subsequent documentation and process information, and final summation of the audit results.

II. AUDIT OVERVIEW

The purpose of the audit was to compare Lilly’s internal clinical trial information provided to SEC against trial registration and trial results information posted through December 31, 2005 on the websites www.LillyTrials.com, www.ClinicalTrials.gov, and www.ClinicalStudyResults.org. For the purposes of this audit, SEC made the assumption that all source information provided to SEC was from a reliable and trustworthy manual or computerized system that had been validated according to industry standards. SEC did not verify the accuracy or completeness of the internal clinical trial information provided by Lilly; nor did SEC perform an audit of Lilly’s clinical trial computer systems, computer system validation documentation, or related processes and procedures. Reference Appendix 2 for a list of terms, acronyms, and references used in this report.

The purpose of the audit was for SEC to determine whether Lilly was adhering to the following criteria defined in the Lilly public statement:

- The applicable trials were posted (applicability)
- The trials were posted during the required timeframe (timeliness)
- The required information for each trial was posted correctly (accuracy and completeness)

SEC divided the audit into three categories: Initiated Trials (New and Ongoing), Clinical Trial Results, and Clinical Trial Results (retrospective studies) as follows:

- **Initiated Trials** includes phase II, III, and IV clinical trials initiated on or after July 1, 2005 (new trials) or phase II, III, and IV clinical trials that were initiated before July 1, 2005 but had not completed on July 1, 2005 (ongoing). Initiated trials are posted to www.LillyTrials.com and www.ClinicalTrials.gov.
- **Clinical Trial Results** includes Phase I, II, and III trials in support of a products’ initial registration, where the first approval for the first indication anywhere in the world occurred on or after July 1, 2004. This category also includes all phase II, III, and IV trials that were completed for marketed products where the trial completed on or after July 1, 2004. Clinical Trial Results are posted to www.LillyTrials.com and www.ClinicalStudyResults.org.
- **Clinical Trial Results (retrospective studies)** includes the core safety and efficacy trials for a product where its first approval for its first indication anywhere in the world occurred between July 1, 1994 and June 30, 2004. Clinical Trial Results (retrospective) are posted to www.LillyTrials.com and www.ClinicalStudyResults.org.

\(^5\) The Clinical Trial Registry Audit Scope and Approach document contains proprietary information of Lilly and SEC and is therefore not included with this Executive Summary.
A summary flow chart is provided in Appendix 3. The approval of the Clinical Trial Registry Audit Scope and Approach document signified that both SEC and Lilly agreed on which trials would be in scope. The scope and approach document also defined the audit criteria and the source documentation against which the audit would be conducted. Because the CTR web sites can be updated at any time, the SEC audit consisted of a point-in-time verification of the three web sites. A point-in-time verification can only provide a snapshot of the level of compliance on the date(s) assessed. By definition, a point-in-time audit does not provide any information regarding past or future compliance status.

A. **Applicability**

For all three audit categories, SEC used various sources of information from Lilly to determine if the applicable trials had been posted. Source documentation was prepared and provided to assist each SEC auditor in determining whether the applicable trials were posted to the appropriate websites.

B. **Timeliness**

SEC was limited to reviewing the website posting dates on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) only, as posting dates are not displayed on the websites [www.LillyTrials.com](http://www.LillyTrials.com) or [www.ClinicalStudyResults.org](http://www.ClinicalStudyResults.org). Although Lilly does not track or display posting dates on its website [www.LillyTrials.com](http://www.LillyTrials.com), they were able to provide internal documentation and screen prints demonstrating the posting dates for results and results (retrospective) on [www.LillyTrials.com](http://www.LillyTrials.com). Specific timeliness dates are defined in each subsection below.

C. **Accuracy and Completeness**

Certain aspects of posted clinical trials contain information that require a degree of subjective decision-making or judgment to be made based on medical or specialized clinical expertise. Therefore, SEC defined the subjective and non-subjective (objective) fields for each audit category prior to the audit, and placed out of scope all components that required a judgment based on medical or specialized clinical expertise. While the scope of the audit included subjective and non-subjective fields, the subjective fields were only assessed for whether data was entered into the field (completeness), and not whether the data entered was accurate. In certain instances, a subjective determination was needed for one or more of the fields previously defined as non-subjective (objective). In these instances, SEC allowed Lilly to provide information from an internal subject matter expert to verify in writing whether the posted data matched the source data. In instances where the information provided by Lilly’s subject matter expert was, in SEC’s judgment, sufficient to verify that the posted data matched the source data, SEC did not include this as a discrepancy in the audit report. Refer to Appendix 4 for a listing of assumptions, clarifications, and conditions used by SEC when auditing accuracy and completeness.

D. **Out of Scope**

1. With respect to all trials audited, SEC made no determinations or judgments regarding safety results. In other words, safety assessments were outside the scope of the SEC audit.
2. SEC did not audit any trials outside of the criteria established in the Lilly public statement. This includes additional trials which Lilly determined it would post due to safety concerns and/or customer interests.
3. SEC did not audit trials that were a result of an industry alliance or cooperation with another group, where the other organization maintains responsibility for posting.

4. Under certain circumstances, posting trial results could contravene national laws or regulations. However, SEC did not make this determination or use this as a criterion to determine which trials to audit.

5. SEC made no determinations or judgments regarding whether a clinical trial’s results revealed significant safety findings.

6. SEC considered publications (citations) to be out of scope.

III. AUDIT RESULTS OVERVIEW

A. General Overview

1. Applicability

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trials in Scope</th>
<th>Number of Nonconforming Trials</th>
<th>Percent of Compliant Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated New Trials</td>
<td>23</td>
<td>0</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Initiated Ongoing Trials</td>
<td>162</td>
<td>0</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Clinical Trial Results</td>
<td>11</td>
<td>0</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Clinical Trial Results (Retrospective)</td>
<td>46</td>
<td>0</td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

2. Timeliness

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trials in Scope</th>
<th>Number of Nonconforming Trials</th>
<th>Percent of Compliant Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated New Trials</td>
<td>23</td>
<td>1</td>
<td>95.7 %</td>
</tr>
<tr>
<td>Initiated Ongoing Trials</td>
<td>162</td>
<td>0</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Clinical Trial Results</td>
<td>11</td>
<td>1</td>
<td>90.9 %</td>
</tr>
<tr>
<td>Clinical Trial Results (Retrospective)</td>
<td>46</td>
<td>0</td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

3. Accuracy and Completeness

The audit for accuracy and completeness was performed based on pre-defined and agreed upon data fields. The data fields audited for both initiated trials and trial results were further categorized based on the subjective and non-subjective nature of the data in each field. Reference the Accuracy andCompleteness section above (section II.C) and Appendix 4 for further explanation and clarification.
Non-Subjective Field Results

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trials in Scope</th>
<th>Total Number of Non-subjective Fields</th>
<th>Total Number of Field Discrepancies</th>
<th>Percent of Compliant Fields</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated New Trials</td>
<td>23</td>
<td>253</td>
<td>9</td>
<td>96.4%</td>
</tr>
<tr>
<td>Initiated Ongoing Trials</td>
<td>162</td>
<td>1782</td>
<td>63</td>
<td>96.5%</td>
</tr>
<tr>
<td>Clinical Trial Results</td>
<td>11</td>
<td>242</td>
<td>6</td>
<td>97.5%</td>
</tr>
<tr>
<td>Clinical Trial Results (Retrospective)</td>
<td>46</td>
<td>1012</td>
<td>22(^7)</td>
<td>97.8%</td>
</tr>
</tbody>
</table>

Subjective Field Results

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trials in Scope</th>
<th>Total Number of Subjective Fields</th>
<th>Total Number of Field Discrepancies</th>
<th>Percent of Compliant Fields</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated New Trials</td>
<td>23</td>
<td>230</td>
<td>1</td>
<td>99.6%</td>
</tr>
<tr>
<td>Initiated Ongoing Trials</td>
<td>162</td>
<td>1620</td>
<td>1</td>
<td>99.9%</td>
</tr>
<tr>
<td>Clinical Trial Results</td>
<td>11</td>
<td>33</td>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>Clinical Trial Results (Retrospective)</td>
<td>46</td>
<td>138</td>
<td>0</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

B. Initiated Trials Summary

The initiated trials category of the audit was divided into two subcategories: new trials (initiated on or after July 1, 2005) and ongoing trials (those initiated prior to July 1, 2005, but not completed as of July 1, 2005).

1. Initiated New Trials

*Applicability:*
SEC reviewed a Lilly report (source documentation) that was generated based on the following criteria:
- Trials with Actual First Patient Visit (aFPV) from July 1, 2005 through December 31, 2005.
- Trials that were Phase II, II/III, III, III/IV, IIIb, and IV.
- Certain trial categories were excluded, such as investigator-initiated, non-interventional, exploratory, and in-vitro categories.

The resulting list included 23 trials which SEC included in the scope of the audit for timeliness, accuracy, and completeness.

---

\(^6\) The summary statistics for Non-subjective Fields for Initiated Trials (New and Ongoing) do not contain the data associated with the Trial Location field. Refer to the Initiated Trials Summary section of the report (and item 1 in Appendix 4) for an explanation and review of the Trial Location results.

\(^7\) 18 of these 22 discrepancies are due to the trials not posting the number of planned patients. If these discrepancies were not listed, the percent compliance for Clinical Trial Results (Retrospective) would be 99.6%.
All trials within scope that should have been posted were posted.

**Timeliness:**
Initiated new trials are to be posted within 21 days of aFPV. Day 1 is interpreted to be the day after aFPV. The “Record First Received” date on www.ClinicalTrials.gov was used to determine the posting date. Because www.LillyTrials.com does not carry a posting date, timeliness was not verified on that website.

One trial out of the 23 was not posted by the expected date. The aFPV for this trial was July 13, 2005, yielding an expected posting date no later than August 3, 2005. The actual posting date was August 19, 2005.

**Accuracy and Completeness**
Refer to Appendix 4 for a listing of the assumptions, clarifications, and conditions used while auditing for accuracy and completeness. A total of 23 trials were reviewed. For each trial, the following non-subjective fields were assessed for accuracy and completeness:

- Unique Trial Number
- Trial Registration Date
- Funding Source
- Primary Sponsor
- Point of Contact
- Research Contact Person
- Condition
- Intervention Type / Name
- Study Type
- Recruitment Status
- Trial Phase
- Location of Trial Sites (recruiting sites only)8

For each trial, the following subjective fields were assessed for completeness:

- Secondary Sponsor
- Brief Study Title
- Official Scientific Title of Study
- Inclusion/Exclusion Criteria
- Anticipated Trial Start Date
- Target Sample Size
- Primary Outcome
- Secondary Outcome
- Trial Description
- Trial Purpose

**Summary**
The following results are for both www.ClinicalTrials.gov and www.LillyTrials.com.

Of the 23 trials assessed (22 for Location):

- 2 trials had discrepancies with Interventions.
- 5 trials did not have placebo posted on the websites.
- 2 trials had discrepancies with Trial Phase.
- 1 trial had a discrepancy with Official Scientific Title.
- 3 trials had discrepancies with site Locations.

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8 Refer to item number 1 in Appendix 4 for a description of the criteria used to audit this field.
2. Initiated Ongoing Trials

**Applicability**
SEC reviewed Lilly reports (source documents) that were generated based on the following criteria (to demonstrate when trials began (aFPV) and when they concluded (aLPV)):
- Exclude trials with aLPV on or before July 1, 2005 (not ongoing as of July 1, 2005).
- Include trials with aFPV (actually did start).
- Trials that were Phase II, II/III, III, III/IV, IIIb, and IV.
- Certain trial categories were excluded, such as investigator-initiated, non-interventional, exploratory, and in-vitro categories.

Trials which were closed but not necessarily completed (for example, cancelled, put on hold, or stopped prematurely) before July 1, 2005 were excluded from the scope of this audit, since they were not ongoing.

The resulting list included 162 trials that SEC audited for timeliness, accuracy, and completeness. All trials within scope that should have been posted were posted.

**Timeliness**
Initiated ongoing trials were to be posted by September 13, 2005. The “Record First Received” date on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) was used to determine the posting date. Because [www.LillyTrials.com](http://www.LillyTrials.com) does not include a posting date, timeliness was not verified on that website.

All trials required to be posted by September 13, 2005 met the posting deadline.

**Accuracy and Completeness**
Refer to Appendix 4 for a listing of the assumptions, clarifications, and conditions used while auditing for accuracy and completeness. A total of 162 trials were reviewed. For each trial, the following non-subjective fields were assessed for accuracy and completeness:
- Unique Trial Number
- Trial Registration Date
- Funding Source
- Primary Sponsor
- Point of Contact
- Research Contact Person
- Condition
- Intervention Type / Name
- Study Type
- Recruitment Status
- Trial Phase
- Location of Trial Sites (recruiting sites only)\(^9\)

For each trial, the following subjective fields were assessed for completeness:
- Secondary Sponsor
- Brief Study Title
- Official Scientific Title of Study
- Inclusion/Exclusion Criteria
- Anticipated Trial Start Date
- Target Sample Size
- Primary Outcome
- Secondary Outcome
- Trial Description
- Trial Purpose

\(^9\) Refer to item number 1 in Appendix 4 for a description of the criteria used to audit this field.
Summary
The following results are for both www.ClinicalTrials.gov and www.LillyTrials.com.

Of the 162 trials assessed:
- 8 trials had discrepancies with Point of Contact information.
- 10 trials had discrepancies with Condition.
- 8 trials had discrepancies with Intervention.
- 12 trials did not have placebo posted on the websites.
- 11 trials had discrepancies with Recruitment Status.
- 14 trials had discrepancies with Trial Phase.
- 6 trials had discrepancies with Location (Using the same criteria described for Initiated Trials, only 51 of the 162 trials were assessed for Location, i.e. actively recruiting).
- 1 trial was missing the posting of an optional field. Upon review of the associated authorization form, it was noted that Lilly approved the decision to not post the data in the field, but the approval signature was 2 days after the compliance date had expired.
- 2 trials did not have a definitive link between the trial number in the protocol and the tracking system. For one of the two trials, Lilly supplied a memo explaining that the trial had undergone a number change, and was in fact the same trial. For the other trial, the protocol did not list a trial number, and the title did not exactly match the tracking system.

C. Clinical Trial Results Audit Summary
The Clinical Trial Results category of the audit was divided into two subcategories: first approvals of first indications and marketed products.

1. First Approvals of First Indications

Applicability
Based on source documentation provided by Lilly, SEC verified that Lilly did not have any products with first approval of first indication anywhere in the world between and including the dates from July 1, 2004 to December 31, 2005. Because there were no applicable trials in this category, this portion of the audit stopped here.

2. Marketed Products

Applicability
SEC reviewed Lilly reports (source documentation) to determine all phase II, III, and IV trials that completed for marketed products between and including the dates from July 1, 2004 to December 31, 2005.

A total of 24 trials were identified after applying the criteria noted above. Upon further review of the 24 trials, it was determined that:
- 11 trials should have been posted
- 13 trials should have evidence of publication pending, thus are not posted
All trials within scope that should have been posted were posted, and all trials within scope that were not posted had documented evidence supporting a pending publication (and thus were not supposed to be posted).

**Timeliness**

All applicable trials are required to be posted to www.LillyTrials.com and www.ClinicalStudyResults.org within 1 year of trial completion (aLPV date). Verification of posting date could only be assessed for www.LillyTrials.com. This assessment was based on screen printouts of the posting directory showing the dates that trial information was uploaded to the website. There was no method available for verifying posting dates to www.ClinicalStudyResults.org. A total of 11 trials were reviewed for timeliness.

One trial (out of 11) was not posted by the expected date. The aLPV was on August 4, 2004, yielding a posting date no later than August 4, 2005. The posting source documentation indicates, however, that it was not posted until October 31, 2005.

**Accuracy and Completeness**

Refer to Appendix 4 for a listing of the assumptions, clarifications, and conditions used while auditing for accuracy and completeness. A total of 11 trials were reviewed. For each trial, the following non-subjective fields were assessed for accuracy and completeness:

- Name of Sponsor
- Name of Finished Product
- Name of Active Ingredient
- Title of Study
- Investigators
- Study Centers
- Length of Study
- Phase of Development
- Objectives (primary only)
- Number of Patients Planned and Analyzed
- Test Product
- Dose
- Mode of Administration
- Duration of Treatment
- Reference Therapy
- Reference Therapy Dose
- Reference Therapy Mode of Administration
- Criteria for Efficacy Evaluation
- Criteria for Safety Evaluation
- Statistical Methodology
- Register Number (same as unique trial number)
- Date of Report

For each trial, the following subjective fields were assessed for completeness:

- Methodology
- Diagnosis and Main Inclusion Criteria
- Summary
Summary

Of the 11 trials assessed:

• 7 trials had mismatches that required a subjective determination. Lilly subject matter experts performed a documented review of these mismatches and determined that the posted information conveyed the same message or content as the source document. In these instances, SEC did not count the mismatches as discrepancies.
• 6 trials had no discrepancies.
• 1 trial had the drug name spelled wrong on the entry screen for ClinicalStudyResults.org.
• 1 trial had a mismatch between the posted efficacy criteria and both the protocol and summary efficacy criteria.
• 1 trial indicated two drugs in the study protocol, but the website postings only listed one drug.
• 1 trial had a mismatch between the posted information and the source documents for the length of the study and the phase of development.
• 1 trial had a mismatch between the posted duration of treatment and the protocol duration of treatment. While noted as a discrepancy, this difference was explained by Lilly and is noted to not have a negative impact on the interpretation of the posted information.

D. Clinical Trial Results (Retrospective) Audit Summary

Applicability

Applicability for Clinical Trial Results (Retrospective) was based on two Lilly memos. The first, dated 03 November 2005, detailed which trials would be categorized as Core Safety and Efficacy trials as well as Additional Optional trials. The intent of the audit was to only assess the Core Safety and Efficacy trials. A second memo, dated 11 March 2006, was created by Lilly to further filter the original listing to only those trials that were posted based on Core Efficacy and Safety. SEC’s audit assumption was that both the original memo and the 11 March 2006 memo would be considered as the source documentation. A total of 47 trials were identified as being in scope using these source documents.

All trials within scope that should have been posted were posted. For the one trial within scope that was not posted, there was documented evidence supporting a pending publication (and thus it was not supposed to be posted).

Timeliness

All Clinical Trial Results (Retrospective) were required to be posted to www.LillyTrials.com and www.ClinicalStudyResults.org by 01 July 2005. Verification of posting date could only be assessed for www.LillyTrials.com. This assessment was based on screen printouts of the posting directory showing the dates that trial information was uploaded to the website. There was no method available for verifying posting dates to www.ClinicalStudyResults.org. A total of 46 trials were reviewed for timeliness.

All trials required to be posted by 01 July 2005 met the posting deadline.
**Accuracy and Completeness**

Refer to Appendix 4 for a listing of the assumptions, clarifications, and conditions used while auditing for accuracy and completeness. A total of 46 trials were reviewed. For each trial, the following non-subjective fields were assessed for accuracy and completeness:

- Name of Sponsor
- Name of Finished Product
- Name of Active Ingredient
- Title of Study
- Investigators
- Study Centers
- Length of Study
- Phase of Development
- Objectives (primary only)
- Number of Patients Planned and Analyzed
- Test Product
- Dose
- Mode of Administration
- Duration of Treatment
- Reference Therapy
- Reference Therapy Dose
- Reference Therapy Mode of Administration
- Criteria for Efficacy Evaluation
- Criteria for Safety Evaluation
- Statistical Methodology
- Register Number (same as unique trial number)
- Date of Report

For each trial, the following subjective fields were assessed for completeness:

- Methodology
- Diagnosis and Main Inclusion Criteria
- Summary

**Results Summary**

Of the 46 trials assessed:

- 22 trials had no discrepancies.
- 23 trials had mismatches that required a subjective determination. Lilly subject matter experts performed a documented review of these mismatches and determined that the posted information conveyed the same message or content as the source document. In these instances, SEC did not count the mismatches as discrepancies.
- 1 trial was incorrectly posted on [www.ClinicalStudyResults.org](http://www.ClinicalStudyResults.org). The website posted the trial summary for another trial instead.
- 18 trials did not list the number of planned patients. SEC listed this as a discrepancy based on the predefined audit criteria described in the Clinical Trial Registry Audit Scope and Approach document. It should be noted, however, that many of these trials predate the ICH E3 recommendation to list the number of planned patients.
- 1 trial had a mismatch between the website(s) posted number of study centers and the protocol or summary number of study centers.
- 2 trials had a mismatch between the website(s) posted number of investigators and the protocol or summary number of investigators.
IV. APPENDIX 1 – LILLY PUBLIC STATEMENT

Principles of Medical Research, Clinical Trial Registry

Eli Lilly and Company is committed to principles of medical research that define the ethical conduct, funding, and communication of clinical research. Lilly conducts clinical research with the highest standards of scientific integrity and respect for patients. Lilly discloses publicly all medical research results that are significant to patients, health care providers or payers – whether favorable or unfavorable to a Lilly product - in an accurate, objective and balanced manner in order for our customers to make more informed decisions about our products. The standards described below represent our commitment to serve patients through transparent and comprehensive disclosure of clinical trial data.

Standards for Disclosure of Lilly Clinical Trial Data:

Clinical Trial Initiation: All Phase II, III and IV trials will be registered at initiation on the Lilly Clinical Trial Registry www.LillyTrials.com, and an independent public registry such as www.ClinicalTrials.gov. These registrations will be done in compliance with the following laws and organization standards: Section 113 of the FDA Modernization Act of 1997 (FDAMA), World Health Organization (WHO) Technical Consultation on Clinical Trials Registration Standards, 25-27 April, 2005, Joint Global Pharmaceutical Industry Position and the Pharmaceutical Research and Manufacturers of America (PhRMA). In all cases, consistent with the above guidelines, the following information will be provided: unique trial number, trial registration date, secondary identifiers, funding source(s), primary and secondary sponsors, responsible contact person, research contact person, brief title, research ethics review, condition, key inclusion and exclusion criteria, study type, anticipated trial start date, and recruitment status. For some studies, additional information will also be disclosed at study initiation. For each study registered at initiation, Lilly will also publicly disclose the results of that study as described below.

Clinical Trial Results: The results of all Phase I, II, and III trials conducted in support of a product’s initial registration will be disclosed on the publicly accessible websites www.LillyTrials.com and www.ClinicalStudyResults.org, regardless of outcome, no later than when the first indication is approved and the drug is commercially available for patient use anywhere in the world. The results of all subsequent Phase II, III, and IV trials conducted after initial approval will be similarly disclosed within one year of trial completion. A trial’s results, irrespective of study phase, will be disclosed as soon as possible if there are any significant safety findings. The registry will also be populated with the results of core efficacy and safety registration trials for products first approved after July 1, 1994. Consistent with ICH E3 guidelines, Lilly will disclose the results of primary and secondary outcome measures that are specified in the study protocol, as well as additional safety and efficacy results that impact patient care and the use of our products. Also, Lilly discloses a comprehensive description of the trial design and methodology for each study. Results will be disclosed regardless of whether they support the hypothesis being tested or are contrary to the predicted outcome. Clinical trial results will be publicly disclosed as stated above, unless posting would compromise publication in a peer-reviewed medical journal or contravene national laws or regulations. Results of studies that are under review by peer-reviewed medical journals that prohibit pre-publication disclosure will be posted on the registry at the time of publication. Clinical trial results are also disclosed through presentations and abstract submissions at professional scientific meetings.

Effective Date: Lilly will comply with these standards for disclosing results for all clinical trials completed after July 1, 2004. Lilly will comply with these standards for disclosing trial initiation for all new studies beginning after July 1, 2005 and for all ongoing trials by September 13, 2005. Results of core efficacy and safety registration trials for products first approved after July 1, 1994 will be disclosed by July 1, 2005.

Verification of Disclosure: An independent third party will audit and verify Lilly’s adherence to these standards of disclosure.

Revised September 2005
# V. APPENDIX 2 – DEFINITIONS, ACRONYMS, AND REFERENCE DOCUMENTATION

## Definitions
For this audit, the following terms were defined:

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accurate</strong></td>
<td>The content posted on the website(s) matches the content of the source document. The term “correct” is also used to mean the same as accurate.</td>
</tr>
<tr>
<td><strong>Clinical Trial</strong></td>
<td>Any investigation in humans intended to discover or verify the effects of an investigational drug or new use of an already marketed drug, and/or to identify any adverse reactions to the investigational drug with the object of determining safety and/or efficacy of the studied use. The terms “clinical trial” and “clinical study” are synonymous.</td>
</tr>
<tr>
<td><strong>Commercially Available</strong></td>
<td>The date the product first leaves a Lilly facility for the purpose of becoming available for commercial use (available to customers).</td>
</tr>
<tr>
<td><strong>Complete</strong></td>
<td>The required fields exist and are populated (per the Lilly public statement) on the website(s). This is not a judgment of accuracy of the fields.</td>
</tr>
<tr>
<td><strong>Core Registration Studies</strong></td>
<td>Studies upon which label claims are based for primary safety and efficacy (also known as pivotal or confirmatory trials).</td>
</tr>
<tr>
<td><strong>Drug Product</strong></td>
<td>A finished dosage form (e.g., tablet, capsule, solution) that contains an active drug ingredient, generally but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is instead to be used as placebo.</td>
</tr>
<tr>
<td><strong>Initial Registration</strong></td>
<td>When the first indication is approved for patient use anywhere in the world.</td>
</tr>
<tr>
<td><strong>Lilly Product</strong></td>
<td>For purposes of this audit, a Lilly product is defined as a drug product where the associated clinical trials are sponsored by Lilly, and Lilly owns the IND and/or NDA.</td>
</tr>
<tr>
<td><strong>Marketed Drug</strong></td>
<td>A drug product for which marketing authorization has been granted in at least one indication in a particular country by a government health agency. Once initial marketing approval is obtained, subsequent research may be ongoing for additional indication or formulations or as part of required safety follow up.</td>
</tr>
</tbody>
</table>
**MeSH term**

MeSH (Medical Subject Headings) is the National Library of Medicine's controlled vocabulary thesaurus. It consists of sets of terms naming descriptors in a hierarchical structure that permits searching at various levels of specificity.

**Non-subjective/**

(Non-subjective)

Basing a decision on existing facts that can be verified without having to make a professional judgment based on experience or knowledge of the facts.

**Ongoing Study**

A clinical trial that was initiated before July 1, 2005 and was not complete on July 1, 2005.

**Protocol**

A written action plan for a clinical trial. The plan states what will be done in the study and why. It outlines how many participants will take part in the study, what types of patients may take part, what tests they will receive and how often, what the treatment plan is, and the sponsor’s plan to analyze the data when the study is completed.

**Protocol Registration System (PRS)**

The computerized system used to enter data for posting to www.ClinicalTrials.gov.

**Public Statement**

The Lilly document titled “Principles of Medical Research Clinical Trial Registry” dated September 2005. This document discusses the disclosure standards and dates that Lilly has committed to comply with regarding clinical trial data. Also referred to as the white paper.

**Publication / (Scientific Publication)**

Any published form of public disclosure of scientific/medical data or scientific/medical opinion or review, whether in print or electronic form. For purposes of this audit, this will also be referred to as citations.

**Subjective**

Basing a decision on experience and individual knowledge as opposed to matching the exact contents of fields.

**Trial Alias**

A unique identifier for the trial being studied.

**Trial Completion**

Equivalent to the actual Last Patient Visit (aLPV).

**Trial Initiation**

Equivalent to the actual First Patient Visit (aFPV).

**www.ClinicalStudyResults.org**

PhRMA created and maintains this web-based data repository for clinical study results to provide public access to clinical trial results.

**www.ClinicalTrials.gov**

The U.S. National Institutes of Health (NIH), through its National Library of Medicine (NLM), developed ClinicalTrials.gov to provide public access to information on initiated clinical research trials.

**www.LillyTrials.com**

The clinical trial registry and results database hosted by Eli Lilly and Company for Lilly products.
Acronyms

- aFPV: Actual first patient visit (indicates trial has started).
- aLPV: Actual last patient visit (indicates trial has completed).
- CTR: Clinical Trial Registry
- ICH: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
- IFPMA: International Federation of Pharmaceutical Manufacturers & Associations
- NLM: National Library of Medicine
- PhRMA: Pharmaceutical Research and Manufacturers of America
- WHO: World Health Organization

Reference Documents
1. Section 113 of the FDA Modernization Act of 1997
2. WHO Technical Consultation on Clinical Trials Registration Standards, 25-27 April 2005
3. IFPMA- Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases, January 6, 2005
4. ICH E3, Guideline for Industry, Structure and Content of Clinical Study Reports, July 1996
6. Principles of Medical Research, Clinical Trial Registry Standards for Disclosure of Lilly Clinical Trial Data, Eli Lilly and Company, September 2005 (otherwise referred to as Lilly’s Public Statement)
VI. APPENDIX 3 – AUDIT FLOW CHARTS

A. Initiated Trials

The following flow chart represents the tasks identified to audit based on the Lilly public statement. Specific information regarding the details and internal source documentation used to audit against is documented in the Clinical Trial Registry Audit Scope and Approach document.

1. Study initiation is defined as the date of actual First Patient Visit (FPV).
2. Although the Lilly white paper indicates compliance for trials initiated after July 1, 2005, Lilly intended for compliance to be on or after July 1, 2006. SEC performed the audit according to Lilly’s intentions and Lilly will reflect this change in future revisions to the white paper.
3. Study completion is defined as the date of actual Last Patient Visit (LPV).
4. See Reference #3 for the 21 day posting requirement.
B. Trial Results

The following flow chart represents the tasks identified to audit for trial results based on the Lilly public statement. Specific information regarding the details and internal source documentation used to audit against is documented in the Clinical Trial Registry Audit Scope and Approach document.

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1. Although the Lilly public statement indicates compliance after July 1, 2004, Lilly intended for compliance to be on or after July 1, 2004. SEC audited according to Lilly’s intentions, and Lilly will reflect this change in future revisions to the Lilly public statement.

2. Commercially available is defined as the date the product first leaves a Lilly facility for the purpose of becoming available to the customers.

3. Study completion is defined as the date of actual Last Patient Visit (LPV).

4. SEC could not verify posting dates on ClinicalStudyResults.org or LillyTrials.com, as there were no dates listed on the websites. SEC did audit the posting dates for LillyTrials.com based on other source documentation that Lilly supplied during the audit.
C. **Trial Results (Retrospective)**

The following flow chart represents the tasks identified to audit for trial results (retrospective) based on the Lilly public statement. Specific information regarding the details and internal source documentation used to audit against is documented in the Clinical Trial Registry Audit Scope and Approach document.

1. SEC could not verify posting dates on ClinicalStudyResults.org or LillyTrials.com as there are no dates listed on the website. SEC did audit the posting dates to LillyTrials.com based on internal source documentation provided during the audit.
VII. APPENDIX 4 – AUDIT ASSUMPTIONS, CLARIFICATIONS, AND CONDITIONS

A. Initiated Trials (New and Ongoing)

While reviewing the content of the non-subjective fields listed in the “Accuracy and Completeness” section for all initiated trials, the following assumptions, clarifications, or conditions were made:

1. Trial site locations are posted when a site is entered into the Lilly tracking system. Each geographic location is posted on the website only once (for example, if there were two sites in Indianapolis, Indiana, then “Indianapolis, IN” appears only once as a location). The sites undergo various status changes, such as “Not Yet Recruiting,” “Recruiting,” and “No Longer Recruiting.” When all sites for a geographic location are no longer recruiting, are completed, or are cancelled, the location may be removed from the website. Because this audit was conducted as a “snapshot” in time, it was not possible for SEC to determine whether all relevant locations for trials had been posted at the appropriate times in the trial life cycle. The site location check, therefore, was made by reviewing active trials only, using sites that had a current status of “Recruiting.” For source documents, SEC used a report provided by Lilly that included current open trials (trials with no actual last patient visit and trials that were not cancelled, on hold, or terminated). Using this criterion, 22 trials in the Initiated New Trials category and 51 trials in the Initiated On-Going Trials category were identified as having a status of “Recruiting” and were reviewed for Location.

2. For some trials, there was no identification information (trial number or trial alias) on the source document which can link it to the Lilly identification in the Lilly tracking system where other information was obtained. In those instances, screen printouts of trial information from the tracking system were provided. Lilly stated that the link could be made by the protocol description and title. SEC noted that in several instances, the titles did not match exactly. Since titles of different trials can be very similar, this mechanism did not always provide a definitive link between the two sources of information. These instances were noted as discrepancies.

3. The Condition field was checked for a match between the study protocol and the websites. Website postings only allow for NLM Medical Subject Headings, thus it may not always be possible to post exact wording from the protocol. Where an exact or very close match was not present, SEC used other sources to make a judgment as to medical equivalency. Lilly indicated that terms used on the websites may convey a broader definition of the studied indication or disease, in order to reach the appropriate set of potential interested study subjects. SEC used other sources to determine that the broader term(s) did in fact include those noted in the source documentation.

4. Product lists were reviewed for equivalency of Intervention information. It was SEC’s expectation that drugs, devices, and behavioral interventions were to be posted. The use of specific vitamins during the trial was not considered an intervention, thus the presence and accuracy of vitamins as Interventions was not verified.

5. For accuracy verifications, trade and generic product names were considered interchangeable.

6. None of the websites provide for posting of “b” Trial Phases (e.g. Phase IIIb). Thus, if the protocol indicated IIIb, for example, and a III was posted, this was determined to be accurate.
7. Some trials combine phases (such as phase II/III or III/IV). Note that www.ClinicalTrials.gov allows for posting of Phase II/III, but not Phase III/IV. In the latter instance, Lilly stated that it was their policy to post the trial as Phase III. (A written procedure formalizing this practice was under development as this report was being written).

8. Due to variations in regional nomenclature (e.g., prefecture in Japan vs. state in the United States), SEC assessed city, state, and country for locations of US trials, and city and country only for international trials. SEC verified these locations against Lilly source documentation. Where exact matches were not present, SEC used its judgment or verified Lilly’s determination of equivalency using other sources. For example, in the source document, one trial listed the city as “Paris CEDEX 20”, while the website posted entry was “Paris.” It was explained that the more specific address is used in the source documentation for the purpose of safety mailings. The more general city term is appropriate for the websites and trial recruiting. Examples of this type were determined to be equivalent. Where it was not possible to determine whether a posting was equivalent, a discrepancy was recorded.

9. Location entries on www.ClinicalTrials.gov must match a predefined list in PRS (the web database entry tool), thus the term used internal to Lilly may not be an exact match for the term listed on the website. In some instances, PRS performs a translation on the entry. For example, an entry of “Russia” is automatically changed to “Russian Federation.” Entries were determined to be equivalent if at least a significant portion of an entry in the Lilly source documentation appeared on the websites. Where additional information appeared on the websites beyond what was in the Lilly source document, a discrepancy was recorded. (For example, the Lilly source lists “Vogelsang”, while the websites list “Volgelsang-Gommern.”)

10. Lilly explained that the Lilly Japanese affiliate enters larger city names or designations into the “state” field in the tracking system, whereas the city field was used for a more detailed breakdown (again, for purposes such as safety mailings). The state and country fields were used to verify website postings for locations in Japan. For example, Tokyo might be entered in the “state” field, and Itabshi-ku might be entered in the “city” field in order to narrow the geographic and population focus.

11. www.ClinicalTrials.gov has multiple areas for contact information for the trial (under the Location and Contact Information section). For purposes of this audit, the Point of Contact non-subjective field was interpreted to be the entry at the top of the Locations list, as well as the individual entries under each geographic location. The Research Contact Person non-subjective field was interpreted to be the “study chairs or principal investigators” information at the bottom of the webpage for each trial. www.LillyTrials.com posts the contact information only in the individual geographic Locations, and this was interpreted to be the Point of Contact field.

12. Lilly posts two general phone numbers (a local number and 800 number) for all trial contacts for both Point of Contact and Research Contact Person.

13. For the non-subjective field Recruitment Status, the Lilly tracking system was used as the source documentation against which the CTR websites were compared. However, once a trial enters a status of “Complete,” it no longer appears on the tracking system report. For trials noted as “Complete” on the websites, the tracking system was checked to confirm that there was an actual last patient visit. If all sites in a trial have an entry noting that the last patient entered treatment, PRS forces a change at the trial level to “No Longer Recruiting,” which may not match the Lilly tracking system status. Such instances were recorded as discrepancies.
14. Fields noted as optional in the WHO Guidance (official scientific title, target sample size, primary outcome, and secondary outcome) are posted by Lilly unless a determination is made not to post. In these instances, a form is signed by the Medical Director authorizing the non-posting of those fields.

15. In some instances, the Official Scientific Title was not posted on www.ClinicalTrials.gov. SEC noted this as a discrepancy, but understands that Lilly did not post the Official Scientific Title in some instances because it was the National Library of Medicine’s policy to not post the Official Scientific Title if it matched the Brief Title exactly. This NLM policy has subsequently changed.

16. In numerous instances (5 in initiated new trials, and 33 in initiated ongoing trials), protocols did not include the Trial Phase. The Lilly tracking system was then used as a secondary source to verify Trial Phase. Lilly stated that the individual responsible for the trial enters the information into the tracking system. Access to this system is limited to only those personnel assigned to the trial.

B. Clinical Trial Results and Clinical Trial Results (Retrospective)

While reviewing the content of the non-subjective fields listed in the “Accuracy and Completeness” section for all trial results, the following assumptions, clarifications, or conditions were made:

1. While reviewing the source documentation against the posted clinical trial results, the following field assumptions were made:
   - “comparator” is equivalent to “reference therapy”
   - “test product” is equivalent to “study drug”
   - “finished product” is equivalent to “marketed drug name”
   - “active ingredient” is equivalent to “generic name”
   - “methodology” is equivalent to “study design”
   - “number of patients analyzed” is equivalent to “number of patients randomized”, unless explicitly stated otherwise

2. The intent of the scope and approach to the audit was to exclude evaluating the content of fields that required specialized medical or clinical judgment. During the course of the audit, however, it was determined that several trials contained fields (categorized prior to the audit as non-subjective) that did not have a precise match between the source documentation and the websites. SEC documented these mismatches as part of the audit. Lilly subject matter experts then performed an internal review of the source document(s) against the website postings to determine whether the posted information conveyed the same message or content as the source document. In instances where the information provided by Lilly’s subject matter expert was, in SEC’s judgment, sufficient to verify that the posted data matched the source data, SEC did not include this as a discrepancy in the audit report.

3. In some instances, the source content or website posting content conveyed a broader representation (i.e., a superset) of the other (e.g., the protocol and synopsis may state “clinical chemistry and urinalysis” for the safety evaluation, while the equivalent field on the website indicates “clinical laboratory data”). While this does not represent an exact match between the fields, SEC did not consider these mismatches to be discrepancies.