**Anonymisation of Clinical Trial Datasets – Eli Lilly and Company**

## 1. Introduction

Providing access to data in ways that allows further research while maintaining the privacy and confidentiality of research participants is critical. There are also privacy laws and regulatory guidance which need to be followed (for example guidance from European data protection regulators and Code of Federal Regulations - Title 45: Public Welfare, Subtitle A §164.514). There are publications in this area which provide guidance.[1,2] The anonymization standard varies under different country's laws. Lilly handles data in accordance with the standard for the country where the data reside. If the country where the data reside has no legal standard, Lilly uses the US standard described in the HIPAA Privacy Rule as the default. Regardless of the local standard, patient initials and date of birth are always removed and investigator-subject number is converted.

This document describes the approach Lilly is using to prepare data for sharing with other researchers in a way that:

- Minimizes risks to the privacy and confidentiality of research participants.
- Ensures compliance with data privacy legal requirements.

## 2. General Approach

Access is provided to anonymised data. Anonymisation involves:

a. **Removing personally identifiable information (PII) from the dataset.** This includes recoding identifiers (by replacing the original code number with a new code number), removing free text verbatim terms, Replacing date of birth with year of birth or age and replacing all dates relating to individual subjects with dummy dates or replacing them with a study day.

b. **Destroying the link (code key) between the dataset that is provided and the original dataset.** Some Data Protection Authorities in Europe suggest that the data can only be considered anonymised if personal information is removed (or redacted) and the subject code number cannot be linked to a research participant. Therefore, research participants' identification code numbers are anonymised by destroying the code key that was used to generate the new code number from the original (i.e. destroying the link between the two code numbers).

[1] Hrynaszkiewicz I, Norton ML, *et al.* Preparing raw clinical data for publication: guidance for journal

editors, authors, and peer reviewers. *BMJ* 2010; **340**: c181.

[2] De-identification of Clinical Trials Data Demystified. *Jack Shostak, Duke Clinical Research Institute (DCRI), Durham, NC http://www.lexjansen.com/pharmasug/2006/publichealthresearch/pr02.pdf*

## 3. Removing personally identifiable information (PII) from the dataset

The 18 identifiers (as defined by HIPAA –see Code of Federal Regulations - Title 45: Public Welfare, Subtitle A §164.514) are removed from the datasets (and related documentation). In addition any other PII that may be present is removed.

This involves removing:

- any names and initials,
- (or recoding) kit numbers and device numbers
- geographic information such as place of work.

In addition the following steps are undertaken:

- Recoding identifiers (or code numbers).
- Removing free text verbatim terms.
- Removing date of birth and supplying age at randomisation**.** Ages above 89 which are aggregated into a single category of "> 89". (This is a specific HIPAA requirement).
- Replacing all original dates relating to individual subjects with randomly generated offsets which are then applied to create 'dummy dates'.
- Reviewing and removing other PII

These steps are described in further detail below.

### *3.1 Recoding Identifiers (or code numbers)*

The following identifiers (code numbers) are re-coded and the code key that was used to generate the new code number from the original code number is destroyed (as described in section 5):

- The investigator identifier (or code number) is re-coded. The investigator name is set to “blank” or dropped from the dataset (see Appendix 1).
- A new subject identifier (or code number) for each research participant.
- Re-code the centre identification number.

- The same new identifiers (or code numbers) are used across all datasets applicable to a single study e.g. raw dataset, analysis-ready dataset. This includes (where applicable) PK datasets, genetic datasets etc.
- Extension studies use the same new identifiers (or code numbers) as used for the initial study to enable individual subject data to remain linked. This also applies to long term follow-up studies where separate reports are published. This is achieved by repeating the data anonymisation process for the initial study data at the same time as the extension/follow up data.

### *3.2 Removing Free Text Verbatim Terms*

Information in a descriptive free text verbatim term may compromise a subject’s anonymity.

- Free text verbatim terms are set to “blank” or dropped from the dataset including:
  - Adverse Events
  - Medications
  - Other e.g. Medical History
  - Other specific verbatim free text

  Certain free text fields may be retained if they do not contain PII and removal of these fields may impact the scientific value of the dataset (e.g. medical history that has not been coded).
- All dictionary coded terms with decode and/or verbatim terms that use a pre-specified list are retained.

### *3.3 Replacing Date of Birth*

Information relating to a research participant’s date of birth and identification of specific ages above 89 may compromise anonymity.

- Date of birth is removed and age at randomisation is supplied with the exception of ages above 89 which are aggregated into a single category of "> 89"

### *3.4 Replacing all Original Dates relating to a Research Participant*

Lilly will use the following method.

#### 3.4.1 Dummy Date Method

Specific dates (other than year) directly related to a research participant may compromise a research participant's anonymity.

All dates are replaced: A random offset is generated for each research participant and applied to all dates for that research participant. All original dates are replaced with the new dummy dates so that the relative times for each research participant are retained.

**Example:** If the original reference date was 01APR2008 and the date of death was 01MAY2008, a random offset is generated (in this case 91 days). Dummy dates are than calculated using this offset of 91 days.

| | **Original Date** | **New Date** | |
|---|---|---|---|
| Reference date | 01APR2008 | 01JUL2008 | Apply offset = 91 days |
| Date of Death | 01May2008 | 31Jul2008 | Apply offset=91 days |
| Relative Time of death | 30 days | 30 days | |

| | Original Date | Reference Date | Study Day |
|---|---|---|---|
| Date of Death | 01May2008 | 01Jan2008 | 122 |

### *3.5 Reviewing and Removing Other PII*

Other data elements that contain PII are removed. For example:

- Information from variable names may contain location information
- Investigator comments may be used to identify a subject
- Genetic data that would enable a direct trace back to an individual subject

Appendix 1: Illustrates non-real examples of how these steps are applied.

## 4. Review and Quality Control

A final review of the HIPAA 18 identifiers is made to determine if further removal is required. Quality Control checks and documentation (QC record) is conducted for the processing of the data and supportive metadata documentation.

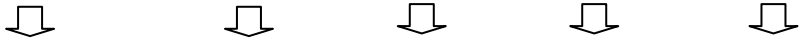
## 5. Destroying the link (key code) between the dataset that is provided and the original dataset

Research participants' identification code numbers are anonymised by replacing the original code number with a new code number (as described in 3.1) and destroying the code key that was used to generate the new code number from the original (i.e. destroying the link between the two code numbers).

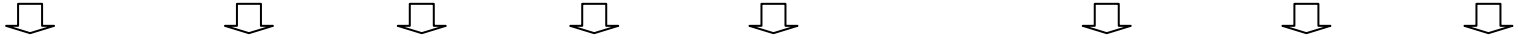
The anonymised datasets are stored in a separate secure location to the original coded datasets.

**Appendix 1: A non-real example illustrating removal of personally identifiable information using the dummy date method**

| Centre ID | Investigator ID (INVID) | Investigator name (INVNAME) | Subject ID (SUBID) | Unique subject ID (USUBID) | Age (yrs) | AE start date | AE end date | Verbatim term |
|---|---|---|---|---|---|---|---|---|
| 00123 | 279344 | Dr Smith | 5 | TJF4392.005 | 57 | 29DEC2010 | 27JAN2011 | Headache |
| 00123 | 279344 | Dr Smith | 2 | TJF4392.002 | 72 | 10JAN2011 | 06APR2011 | Nausea |
| 00123 | 279344 | Dr Smith | 1 | TJF4392.001 | 91 | 25MAR2011 | 12AUG2011 | Cold |
| 00123 | 279344 | Dr Smith | 66 | TJF4392.066 | 89 | 28MAR2011 | 31MAR2011 | Cold |
| 00123 | 279344 | Dr Smith | 8 | TJF4392.008 | 94 | 01MAR2011 | 15MAY2011 | Flu |
| 05678 | 333721 | Dr Jones | 19 | TJF4392.019 | 85 | 14OCT2010 | 20OCT2011 | Cold |
| 05678 | 333721 | Dr Jones | 4 | TJF4392.004 | 53 | 24MAY2011 | . | Headache |
| 05678 | 333721 | Dr Jones | 23 | TJF4392.002 | 76 | 01MAR2011 | 15MAR2011 | Pain |



New INVID | Remove INVNAME | New SUBID | New USUBID | Remove ages above 89 | Add dummy dates | Add dummy dates | Remove



| Centre ID | Investigator ID (INVID) | Investigator name | Subject ID (SUBID) | Unique subject ID (USUSID) | Age (yrs) | | AE start date | AE end date | Verbatim term |
|---|---|---|---|---|---|---|---|---|---|
| 00123 | 227 | | 8754 | TJF4392.8754 | 57 | | 19AUG2010 | 17SEP2010 | |
| 00123 | 227 | | 5681 | TJF4392.5681 | 72 | | 06JUL2010 | 30SEP2010 | |
| 00123 | 227 | | 1475 | TJF4392.1475 | >89 | | 05SEP2010 | 23JAN2011 | |
| 00123 | 227 | | 6589 | TJF4392.6589 | 89 | | 06SEP2010 | 09SEP2010 | |
| 00123 | 227 | | 3562 | TJF4392.3562 | >89 | | 29JUN2011 | 12SEP2011 | |
| 05678 | 208 | | 1457 | TJF4392.1457 | 85 | | 16JUL2011 | 12SEP2011 | |
| 05678 | 208 | | 2214 | TJF4392.2214 | 53 | | 04NOV2010 | . | |
| 05678 | 208 | | 2236 | TJF4392.2236 | 76 | | 01JUL2010 | 15JUL2010 | |