



A New Era: Open Access to Clinical Trial Data

Phuse Conference – Data Transparency stream

London, October 2014

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A New Era: Open Access to Clinical Trial Data



«Data are like children....

You like your own best, and do not like strangers to play with them.»

HG Eichler Oct 2012

Outline

Topics covered in today presentation

1- Fundamentals

- Background and Multisponsor site
- Scope of Documents and Data shared

2- Challenges

- Informed Consent
- Data Anonymization Standards
- Cross-divisional approach
- New Business process and documents involved

3- Implementation

- Overview of Data Sharing Process
- De-identification (vs) Anonymization
- Overview of Anonymization process
- Modes of Anonymization
- Result of Anonymization process

4- Operating Model

- The tripartite strategy: Novartis / MMS Holdings Inc. / The SAS Institute
- Mid term vision

1- Fundamentals

Data Transparency is coming

Much external pressure to reveal clinical trial data



Transparency measures forced on pharma

Chemistry World - Sep 30, 2014

The same is not true for clinical **data**, where **transparency** will have legal force. This is despite the EFPIA and its US counterpart PhRMA ...

Google

data transparency

Web

Images

News

Videos

About 96,700,000 results (0.34 seconds)

Legislative reform of China's healthcare sect

Lexology (registration) - Aug 31, 2014

While developments in high-profile **anti-bribery** investigations into both domestic ...
Indeed, all **pharmaceutical** and medical device companies ...



EU Ombudsman: Clinical trials face new **transparency** challenges

EurActiv - Sep 30, 2014

The Ombudsman warning came just month after the EU adopted a new clinical trials regulation, which obliges **pharmaceutical** companies to share scientific **data** on new medications submitted for approval to the European Medicines Agency (EMA). O'Reilly ...

New EMA policy on access to clinical trial **data** set to be finalised this week

Out-Law.com - Sep 30, 2014

Expert in life sciences Helen Cline of Pinsent Masons said: "There is a whole spectrum of benefits that could arise from making the clinical trial process and clinical trial **data** more **transparent** from improving the efficiency of drug discovery to the public health benefits." Earlier this year, the Council of Ministers and the European Parliament voted in favour of a new Clinical Trials Regulation which will require **pharmaceutical** companies and other medical researchers to post results of all their European clinical trials on a ...



Ben Goldacre
The Sunday Times
bestseller

4th
400+ pages

Novartis joins *ClinicalStudyDataRequest.com*

Joining multi Sponsor site in 2014



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About

This site

Access to the underlying (patient level) data that are collected in clinical trials provides opportunities to conduct further research that can help advance medical science or improve patient care. This helps ensure the data provided by research participants are used to maximum effect in the creation of knowledge and understanding.

Researchers can use this site to request access to anonymised patient level data and supporting documents from clinical studies to conduct further research.

Next steps

[Study sponsors](#) who have committed to use this site are **Bayer, Boehringer Ingelheim, GSK, Lilly, Novartis, Roche, Sanofi** and **ViiV Healthcare**.

Other clinical trial sponsors and funders are invited to join with the aim of transitioning to a fully independent system which allows access to data from clinical trials conducted by multiple companies and organisations. It is hoped that such a system will be put in place as soon as possible.

If you are a study sponsor interested in listing studies on this site, contact information is provided [here](#).

Novartis Internet Site

Available from Study Sponsor's Section on ClinicalStudyDataRequest.com

Clinical Trials

[Home](#)[Clinical study results](#)[Ongoing trials](#)[Patient-level data](#)

Since 2005

Novartis publically shares clinical trial summary results for medicines and vaccines under development and approved by regulatory agencies on the Novartis clinical trial results public website, www.novctrd.com.



Clinical study results

Since 2005, Novartis has made public the summary results of our interventional clinical trials on the Novartis clinical trial results database. »

Ongoing trials

Novartis is currently conducting clinical trials around the world for a number of diseases. Search Novartis-sponsored ongoing interventional clinical trials. »

Patient-level data

Novartis has joined a multi-company online system through which external researchers can request access to anonymized patient-level data from our clinical trials. »

Scope of Documents and Data shared

What do we share?

- After a careful review of the request by an independent review panel, the following data and accompanying trial documentation will be shared with qualified external researchers when available.

Document	Divisional Responsibility
Annotated CRF	Data Management
Original Protocol and any amendments	Clinical Office
Dataset Specifications	Stats & Programming
Original Reporting and Analysis Plan	Stats & Programming
Anonymized raw study datasets	Stats & Programming
Anonymized analysis-ready datasets	Stats & Programming
CSR excluding appendices since these are in patient level data	Medical Writing

Challenges in Data Sharing

Informed Consent

Points of consideration

- Informed Consents have changed over time and may be restricting the use of the data only for the study in question – additionally individual Ethics Committees can propose alterations to ICF and these are not tracked.
- Does anonymization remove the issue of IFC? Currently a legal discussion. Moving forward consent to anonymize the data for use beyond the scope of the trial is added as an option to patients in the ICF. Management of ICF needs to be assessed as many trials do not use the standard ICF but use the site ICF or their own version of an ICF – Need to ensure anonymization is inserted into these ICF's without exception



Challenges around Anonymization

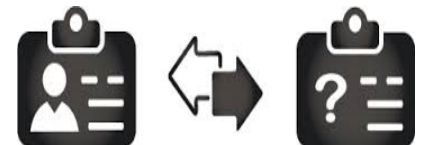
Points of consideration for maintaining within study/patient data relations

Points of consideration

- It is easy to de-identify data but to create an anonymized database that maintains the within study and within patient data relations needed for analyses is more difficult.
- To anonymize the data, we could simply drop all identifying data variables but that would result in a database that is not useful for analyses. There would be no dates, subject IDs, ages, etc.
- So, data needs to be anonymized while retaining the within study and within patient data relations. Dates need to be changed and the intervals between any two dates needs to be the same as in the original (/identified) data.
- Novartis approach is to anonymize (as opposed to de-identify) and destroy translation tables



NVS Data
Anonymization Stand



2- Challenges

Define a new Business process from scratch

Setup SOP/WP, including Standardization

Requires documentation that covers all the divisions

- This involves:
 - SOP and related Working Practices
 - Training and User guidance documents
 - Standards documents
 - Macro validation supportive documentation and Risk assessment (against hacking the lock box and future risk of re-identification with increased access to data through other channels, e.g. Social networks (Article 29 of Directive 95/46/EC Data Protection Working Party WP216 Anonymization Techniques released April 2014))



SOP

Standard Operating Procedures

A single model for all Novartis Divisions*

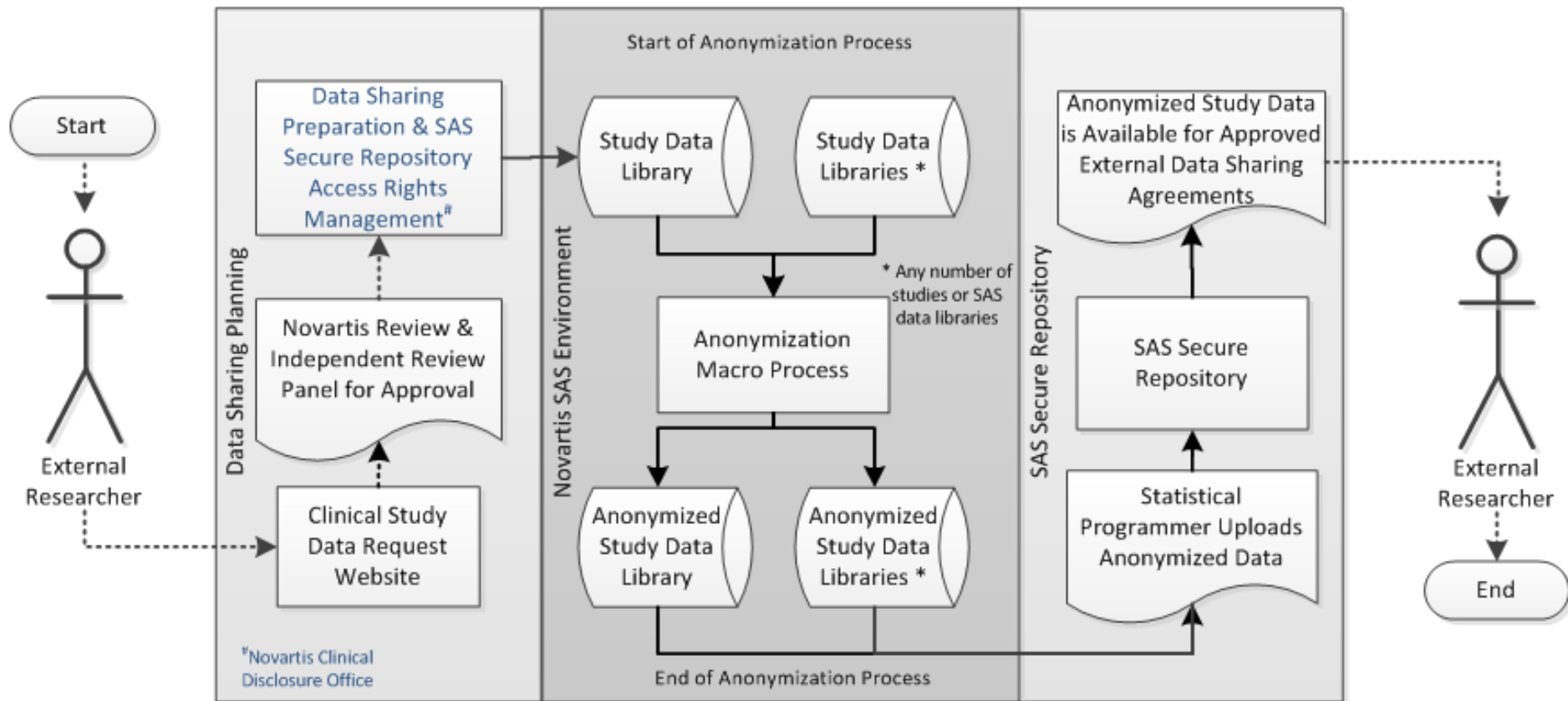
Define a global standard but acknowledging Division specifics

Type and level of anonymization

- *5 Divisions involved (GenMeds, Onc., Alcon, Vaccines, OTC)
- Define a **minimum level** of anonymization required for all data **to meet legal and data privacy protection** and inline with ICF
- Define **Global Standards** for all Divisions
- Establish **one process flow** to anonymize study data from all divisions, involving different programming environment with multiple operating systems
- Heterogeneity of data format within and across Novartis divisions makes it difficult to establish a single model for data anonymization. **Data is shared in its native format.** No conversion to match CDISC or SDTM Standards

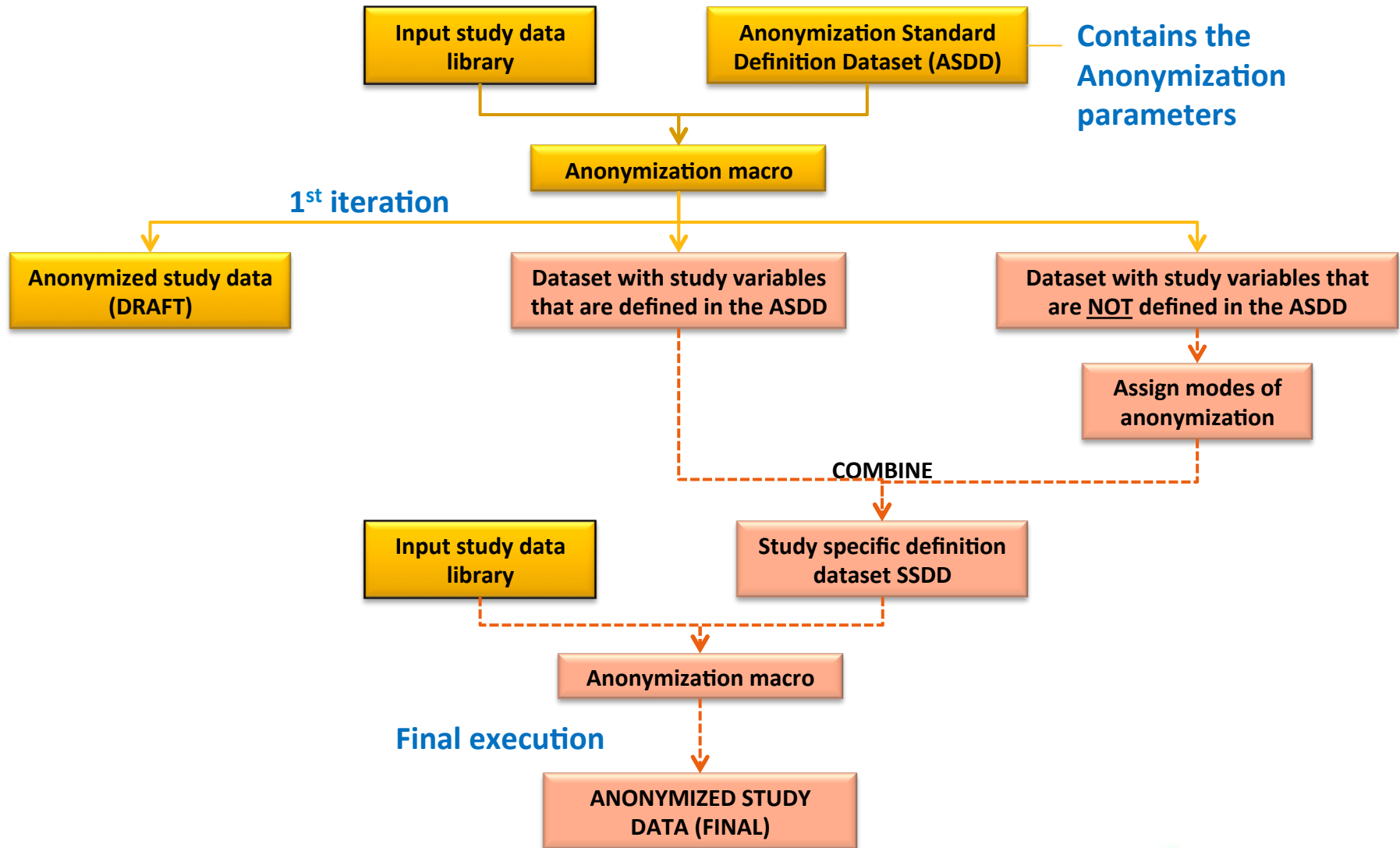


Overview of Data Sharing Process



Overview of Anonymization process

Proposed solution for creating a Study specific definition dataset



An outlook of the Definition Dataset

- ✓ List of all variables from all datasets to be anonymized

DATASET	VARIABLE	LABEL	MODE of anonymization	Identifier_ type	date_type	full_date	TYPE	FORMAT
AEFF2EVT	ACSDT	Date of 1st Hosp. for ACS	DATE	date	sasdate		1	DATE
ACMDATC	CMDEND10	Concomitant med. end date (Oracle date)	DATE	datetime	sasdatetime		1	DATETIME
AAEV	AGECL65	Age group (<65,>=65)	DROP				1	AGE1F_
ACMD	AGECL65	Age group (<65,>=65)	DROP				1	AGE1F_
ACMDATC	AGECL65	Age group (<65,>=65)	DROP				1	AGE1F_
ACMP	ACTTRTC	Actual treatment code	NONE				2	\$
ACOM	ACTTRTC	Actual treatment code	NONE				2	\$
ADAR	ACTTRTC	Actual treatment code	NONE				2	\$
AADJ	CTR1N	Center number	TRANSLATE				1	
AAEV	CTR1N	Center Number	TRANSLATE				1	
ABIO	SID1A	Subject Identifier	TRANSLATE				2	\$
ABKG	SID1A	Subject Identifier	TRANSLATE				2	\$
ACMPDTH	SID1A	Subject Identifier	TRANSLATE				2	\$

- ✓ This is the place where the modes of anonymization are entered
- ✓ The Definition Dataset is standardized at the Division level and is maintained through a change management system (version history and approval process)

Modes of Anonymization

Examples

■ DROP

	TEST_VAR1	TEST_VAR2
1	DATA	data
2	DATA	data
3	DATA	data



	TEST_VAR2	
1	data	
2	data	
3	data	

■ MISSING

	TEST_VAR1	TEST_VAR2
1	DATA	data
2	DATA	data
3	DATA	data



	TEST_VAR1	TEST_VAR2
1		data
2		data
3		data

■ TRANSLATE

	TEST_VAR1	
1	SUBJ01	
2	SUBJ01	
3	SUBJ04	



	TEST_VAR1	
1	XXXXnn	
2	XXXXnn	
3	XXXXnn	

Modes of Anonymization (cont.)

Examples

■ DATE

VIEWTABLE: Rchwork.Input			VIEWTABLE: Rchwork.Output		
	TEST_DT			TEST_DT	
1	06-25-1985		1	07-26-2085	
2	08-16-1986		2	09-17-2086	
3	12-31-1991		3	01-01-2091	

■ AGEINT

VIEWTABLE: Rchwork.Input			VIEWTABLE: Rchwork.Output		
	TEST_AGE			TEST_AGE	
1	60		1	60	
2	96		2	90 or older	
3	55		3	55	

■ NONE (straight copy of the variable)

** By default in the macro, if no mode is defined for a variable, the variable is dropped*

De-identification (vs) Anonymization

Original Dataset

VAR1	VAR2
SUBJ012	01
SUBJ012	02
SUBJ045	03
SUBJ045	04



VAR1	VAR1
SUBJ012	XXXXnn1
SUBJ012	XXXXnn1
SUBJ045	XXXXnn2
SUBJ045	XXXXnn2

Keys table

De-identified Dataset

VAR1	VAR2
XXXXnn1	
XXXXnn1	
XXXXnn2	
XXXXnn2	



Original Dataset

VAR1	VAR2
SUBJ012	01
SUBJ012	02
SUBJ045	03
SUBJ045	04

Novartis Approach

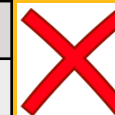


VAR1	VAR1
SUBJ012	XXXXnn1
SUBJ012	XXXXnn1
SUBJ045	XXXXnn2
SUBJ045	XXXXnn2

Keys table

Anonymized Dataset

VAR1	VAR2
XXXXnn1	
XXXXnn1	
XXXXnn2	
XXXXnn2	



Result of Anonymization process

• Example

Study data example on top and anonymized data on bottom after *modes of anonymization* were applied.

Study Data

Center ID	Investigator ID	Investigator name	Subject number	Date of birth	Age (yrs)	AE start date	AE end date	Verbatim term	Preferred term
T1230	279T344	Dr Smith	2002	08Aug1954	57	29DEC2010	27JAN2011	HEADACHE	Headache
T1230	279T344	Dr Smith	2002	08Aug1954	57	10JAN2011	06APR2011	BRONCHITIS	Bronchitis
T1230	279T344	Dr Smith	2004	09Aug1919	92	25MAR2011	12AUG2011	COLD	Nasopharyngitis
T1230	279T344	Dr Smith	2004	09Aug1919	92	28MAR2011	31MAR2011	FLU	Influenza
T1230	279T344	Dr Smith	2004	09Aug1919	92	01MAR2011	15MAY2011	PAIN	Pain
G5670	348G224	Dr Jones	2010	09Aug1947	64	14OCT2010	20OCT2011	ACHE NOS	Pain
G5670	348G224	Dr Jones	2010	09Aug1947	64	24MAY2011		BRONCHIAL INFECTION	Bronchitis
G5670	348G224	Dr Jones	2010	09Aug1947	64	01MAR2011	15MAR2011	CHRONIC PAIN	Pain

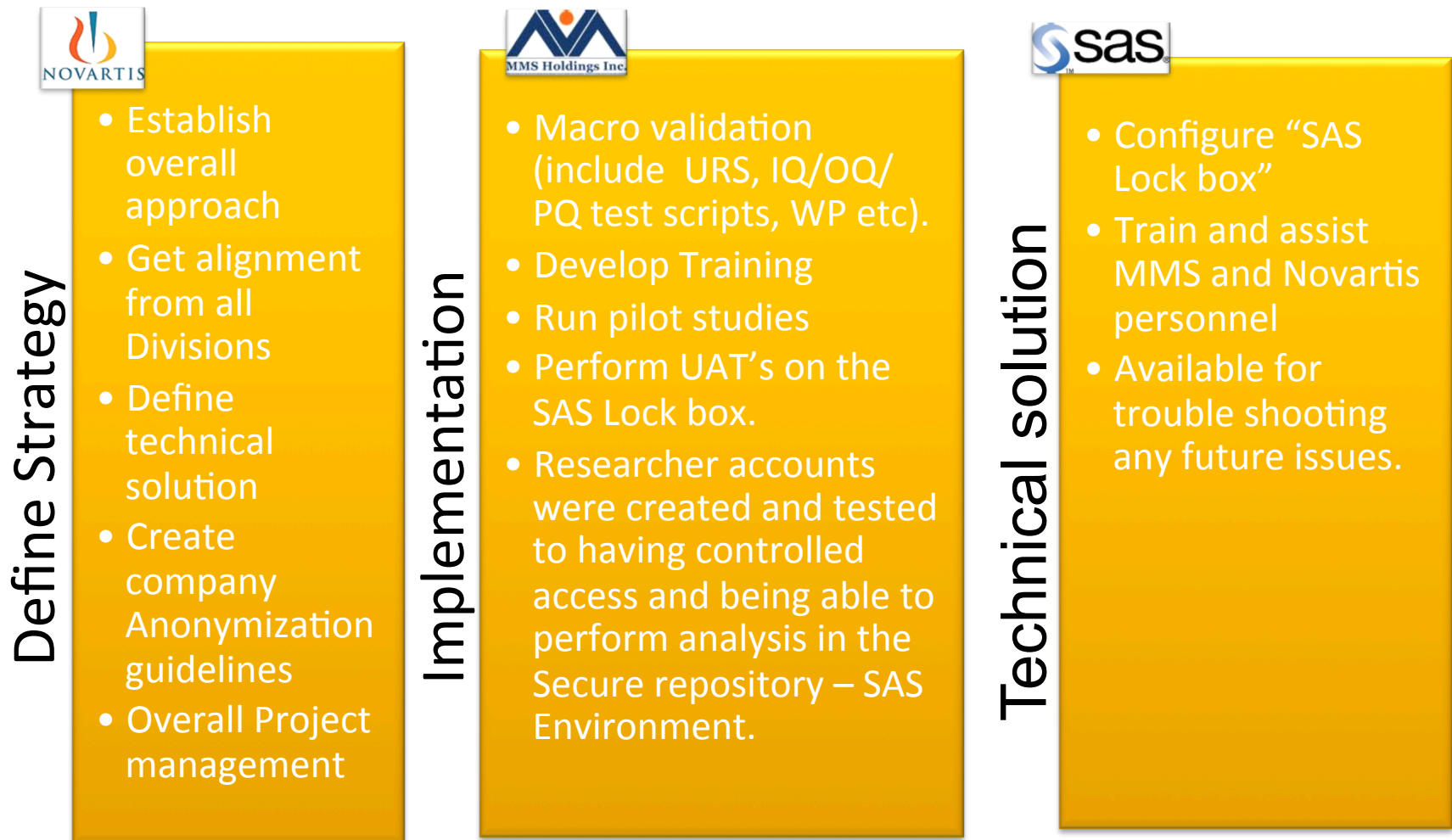
TRANSLATE	TRANSLATE	MISSING	TRANSLATE	DROP	AGEINT	DATE	DATE	MISSING	NONE
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Anonymized Data

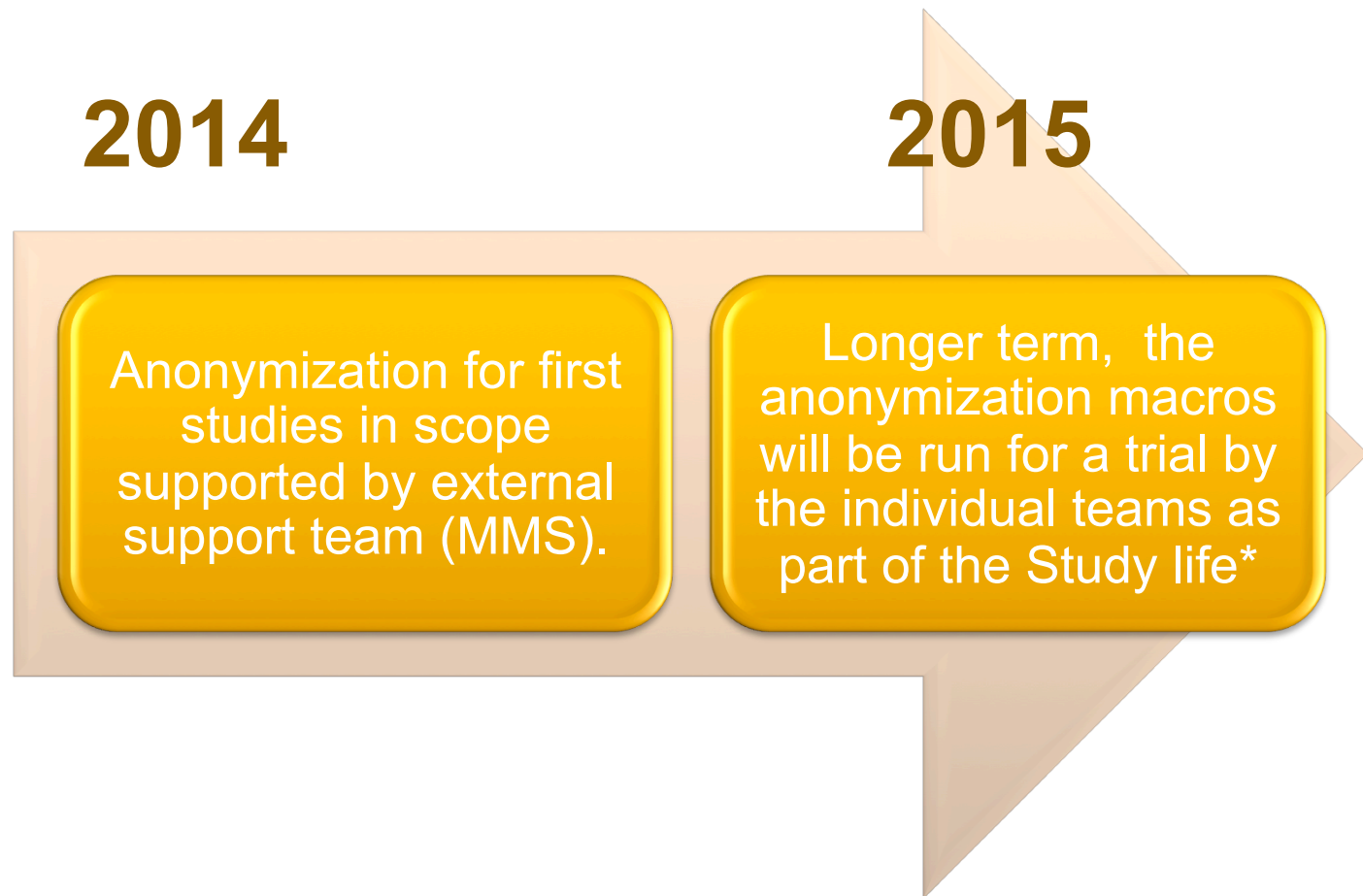
Center ID	Investigator ID	Investigator name	Subject number		Age (yrs)	AE start date	AE end date	Verbatim term	Preferred term
Xnn10	nnnXn10		Ay12		57	16FEB2093	17MAR2093		Headache
Xnn10	nnnXn10		Ay12		57	28FEB2093	25MAY2093		Bronchitis
Xnn10	nnnXn10		Eb65		90 or Older	13MAY2093	30SEP2093		Nasopharyngitis
Xnn10	nnnXn10		Eb65		90 or Older	16MAY2093	19MAY2093		Influenza
Xnn10	nnnXn10		Eb65		90 or Older	19APR2093	03JUL2093		Pain
Xnn11	nnnXn11		Nz97		64	02DEC2092	08DEC2093		Pain
Xnn11	nnnXn11		Nz97		64	12JUL2093			Bronchitis
Xnn11	nnnXn11		Nz97		64	19APR2093	03MAY2093		Pain

The Tripartite Strategy

Novartis, MMS Holding, SAS



Mid term vision *End of 2014 and next year*



* Exact study scope still being assessed

