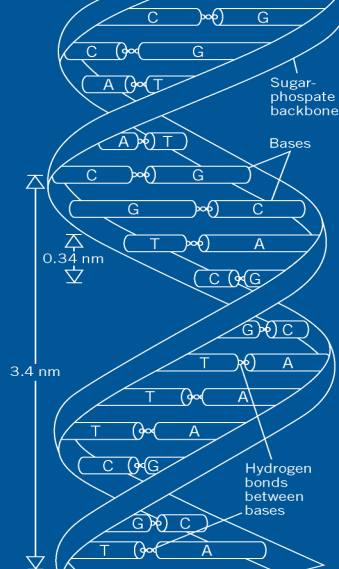




How Do I Map That? - SDTM Implementation Challenges

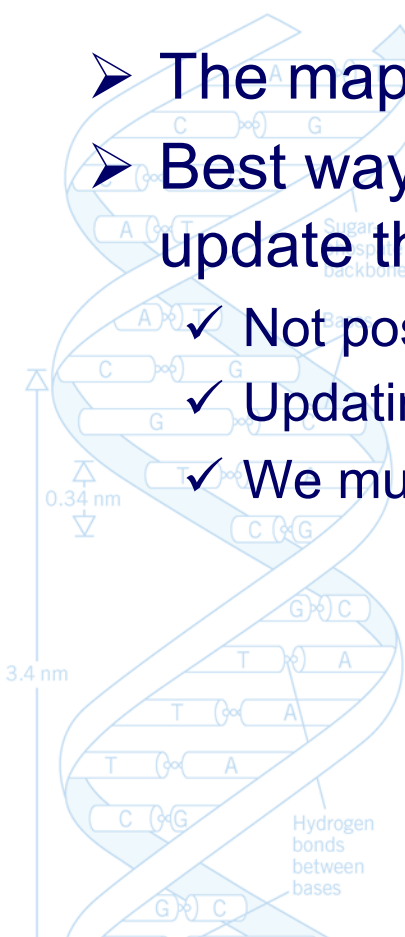
Chris Price, Roche Products Ltd.

October 2010

Agenda

- 
- Background
 - Implementation Examples
 - ✓ Deaths - Events or Outcome?
 - ✓ Tender and Swollen Joint Counts
 - ✓ Interventions to Infusions
 - ✓ Symptoms of Infusion Related Reactions
 - ✓ Smoking History
 - Conclusion

Background

- 
- The mapping from a CRF to SDTM is usually trivial
 - Best way to resolve some mapping challenges is to update the data collection model
 - ✓ Not possible for legacy studies
 - ✓ Updating existing standards can be difficult and takes time
 - ✓ We must have an interim solution

Background

- 
- Presented here are some examples from a Phase III Rheumatoid Arthritis project
 - ✓ The CRFs and operational database had already been finalized prior to the decision to map to SDTM
 - ✓ No programming of analysis had been started
 - Draft SDTM v1.2 and SDTM IG v3.1.2 had just been released for public review
 - Mappings were updated in some instances based on the final versions

Deaths - Events or Outcome?

In the case of patient's death

Death, whether or not related to the study medication(s), must be immediately reported to sponsor by telefax on an SAE form.

Date of death

dd	mm	yy
----	----	----

Primary cause of death _____

Underlying cause of death (if applicable) _____

Relationship of death to study medication

- unrelated ☐
- remote ☐
- possible ☐
- probable ☐

Was autopsy performed? yes ☐
no ☐

If yes, please summarize findings: _____

General comment: _____

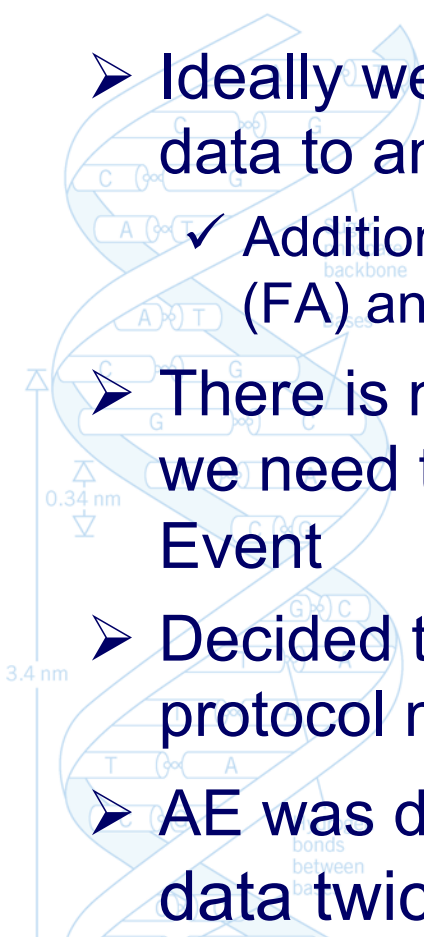
Previously collected
as it's own domain

Data was reconciled
across multiple pages

SDTM considers
death as an outcome
of an event

Psychological impact
of not collecting
deaths separately

Deaths - Events or Outcome?

- 
- Ideally we would update the CRF to explicitly link this data to an individual Adverse Event
 - ✓ Additional information would be mapped to Findings About (FA) and Comments (CO)
 - There is no explicit link between AE and Death pages so we need to treat death in this collection model as an Event
 - Decided that death was not a disposition event or protocol milestone
 - AE was discounted as it would be collecting the same data twice in a single domain

Deaths - Events or Outcome?

In the case of patient's death

Death, whether or not related to the study medication(s), must be immediately reported to sponsor by telefax on an SAE form.

CE.CESTDTC

Date of death dd mm yy **CE.CETERM**

Primary cause of death _____

Underlying cause of death (if applicable) _____ **SUPPCE.QVAL**

Relationship of death to study medication **SUPPCE.QNAM = 'CEDDUTXT'**

unrelated ☐
remote ☐
possible ☐
probable ☐

CE.CEREL

Was autopsy performed? yes ☐ **SUPPCE.QVAL**
no ☐ **SUPPCE.QNAM = 'CEDDAUYN'**

If yes, please summarize findings: _____

_____ **SUPPCE.QVAL**
_____ **SUPPCE.QNAM = 'CEDDAUR'**

General comment: _____

CO.COVAL
CO.RDOMAIN = 'CE'
CO.IDVAR = 'CESEQ'

Decision was to map
to Clinical Events
Domain (CE)

Purpose of CE is to
capture clinical
events of interest not
classified as AEs

Consistent with
capturing death
when AEs not
collected - e.g.
Survival Follow-Up

Tender and Swollen Joint Counts

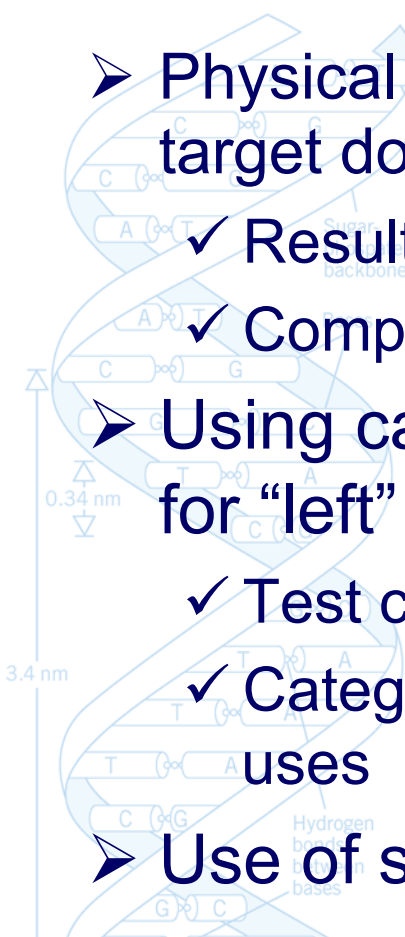
RIGHT
JOINT
LEFT

Tenderness present?	Swelling present?	Not done	Reason if not done	JOINT	Tenderness present?	Swelling present?	Not done	Reason if not done
☐	☐	☐		Shoulder	☐	☐	☐	
☐	☐	☐		Elbow	☐	☐	☐	
☐	☐	☐		Wrist	☐	☐	☐	
☐	☐	☐		MCP1	☐	☐	☐	
☐	☐	☐		MCP2	☐	☐	☐	
☐	☐	☐		MCP3	☐	☐	☐	
☐	☐	☐		MCP4	☐	☐	☐	
☐	☐	☐		MCP5	☐	☐	☐	
☐	☐	☐		IP Thumb	☐	☐	☐	
☐	☐	☐		PIP2	☐	☐	☐	
☐	☐	☐		PIP3	☐	☐	☐	
☐	☐	☐		PIP4	☐	☐	☐	
☐	☐	☐		PIP5	☐	☐	☐	
☐	☐	☐		Knee	☐	☐	☐	

Assessor's initials
Tender joint count
Swollen joint count

- Primary Endpoint for RA study
- Not a natural fit for existing SDTM domains
- Location has two levels of granularity which is not addressed by SDTM

Tender and Swollen Joint Counts

- 
- Physical Examination (PE) sounds like an appropriate target domain for joint measurements
 - ✓ Results would need to be remapped to fit the domain
 - ✓ Complicated to use as part of analysis
 - Using categories (--CAT) or sub-categories (--SCAT) for “left” and “right”
 - ✓ Test codes would appear in both categories
 - ✓ Category variable may be better employed for other uses
 - Use of supplemental qualifiers is best avoided

Tender and Swollen Joint Counts

ZJ.ZJLOC = 'RIGHT' || <JOINT>

ZJ.ZJLOC = 'LEFT' || <JOINT>

RIGHT				JOINT	LEFT			
Tenderness present?	Swelling present?	Not done	Reason if not done		Tenderness present?	Swelling present?	Not done	Reason if not done
☐	☐	☐		Shoulder	☐	☐	☐	
☐	☐	☐		Elbow	☐	☐	☐	
☐	☐	☐		Wrist	☐	☐	☐	
☐	☐	☐		MCP1	☐	☐	☐	
☐	☐	☐		MCP2	☐	☐	☐	
☐	☐	☐		MCP3	☐	☐	☐	
☐	☐	☐		MCP4	☐	☐	☐	
☐	☐	☐		MCP5	☐	☐	☐	
☐	☐	☐		IP Thumb	☐	☐	☐	
☐	☐	☐		PIP2	☐	☐	☐	
☐	☐	☐		PIP3	☐	☐	☐	
☐	☐	☐		PIP4	☐	☐	☐	
☐	☐	☐		PIP5	☐	☐	☐	
☐	☐	☐		Knee	☐	☐	☐	

ZJ.ZJSTAT

ZJ.ZJSTAT

ZJ.ZJREASND

ZJ.ZJREASND

Assessor's initials Tender joint count Swollen joint count

SUPPJZ.QVAL
SUPPJZ.QNAM = 'ZJEVALSP'

ZJ.ZJTESTCD = 'TENDER' or 'SWELLING'
ZJ.ZJTEST = 'TENDERNESS' or 'SWELLING'
ZJ.ZJORRES = 'PRESENT' or 'ABSENT' or null

Decided to map to a sponsor defined findings domain (ZJ)

Straight forward mapping (- - TESTCD, --ORRES, - -STAT and - -REASND)

Granularity of location concatenated in - -LOC

Interventions to Infusions

Start time (24 hr clock) h:min	Stop time (24 hr clock) h:min	Total volume infused (ml)
EX.EXSTDTC	EX.EXENDTC	EX.EXVAMT

EX.EXROUTE = 'INTRAVENOUS'
 EX.EXDOSFRM = 'SOLUTION'
 EX.EXVAMTU = 'ML'

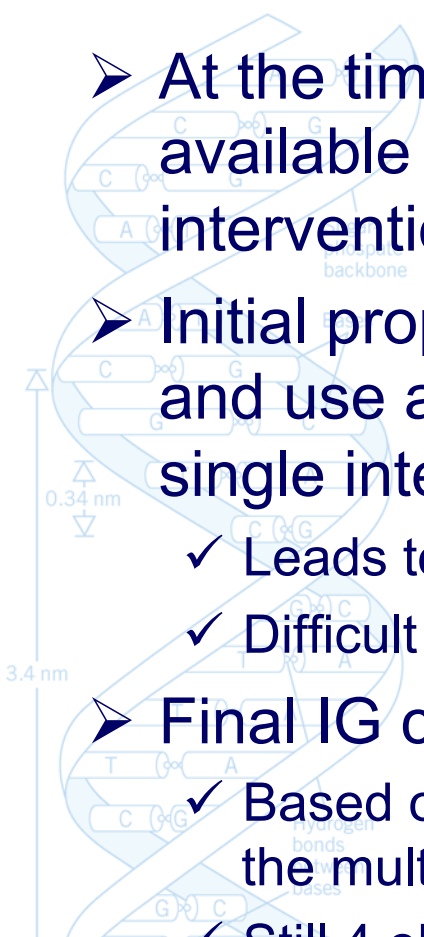
Basic information maps simply to the Exposure domain (EX)

Infusion during this administration was:	Start time of intervention (24 hr clock) h:min	Stop time of intervention (24 hr clock) h:min	Reason
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other

Mapping question arises with the interventions

Multiple fields for each intervention are all related to a single infusion

Interventions to Infusions

- 
- At the time of the initial mapping there were no solutions available for relating these multiple fields for each interventions to a single infusion
 - Initial proposal was to limit QNAM values to 6 characters and use a numeric suffix to group fields relating to a single intervention
 - ✓ Leads to complicated mapping as would be better as 2 variables
 - ✓ Difficult to use the mapping in any analysis
 - Final IG contained the Findings About (FA) domain
 - ✓ Based on the above mapping FAGRPID could be used to link the multiple fields for each intervention together
 - ✓ Still 4 observations per intervention

Interventions to Infusions

Start time (24 hr clock) h:min	Stop time (24 hr clock) h:min	Total volume infused (ml)
EX.EXSTDTC	EX.EXENDTC	EX.EXVAMT

EX.EXROUTE = 'INTRAVENOUS'
 EX.EXDOSFRM = 'SOLUTION'
 EX.EXVAMTU = 'ML'

Intervention Information is mapped to Findings About (FA)

FA.FAOBJ = 'INFUSION INTERVENTION'

Infusion during this administration was:	Start time of intervention (24 hr clock) h:min	Stop time of intervention (24 hr clock) h:min	Reason
FA.FAORRES	FA.FASTDTC	FA.FAENDTC	SUPPFA.QVAL SUPPFA.QNAM = 'MODREAS'
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other
1 ☐ slowed down 2 ☐ interrupted 3 ☐ discontinued			1 ☐ adverse event 2 ☐ infusion related reaction 3 ☐ other

Use start and end time variables and map the reason for intervention to a SUPPQUAL

Records in RELREC are needed to relate EX records to FA

FA.FATESTCD = 'TXINT' FA.FATEST = 'TYPE OF INFUSION INTERRUPTION'

Symptoms of Infusion Related Reactions

Infusion related reactions that occur between start of study medication infusion and within 24 hours of the completion of the study medication infusion should be recorded here.

Event: Infusion related reaction **AE.AETERM**

Is this a serious infusion related reaction (see definition in protocol)?

Date of onset

dd	mm	yy
----	----	----

AE.AESTDTC

Time of onset (24 hour clock)

h	min
---	-----

yes ☐ → complete SAE form within one working day of occurrence and fax immediately to the sponsor
no ☐

AE.AESER

Infusion related reaction

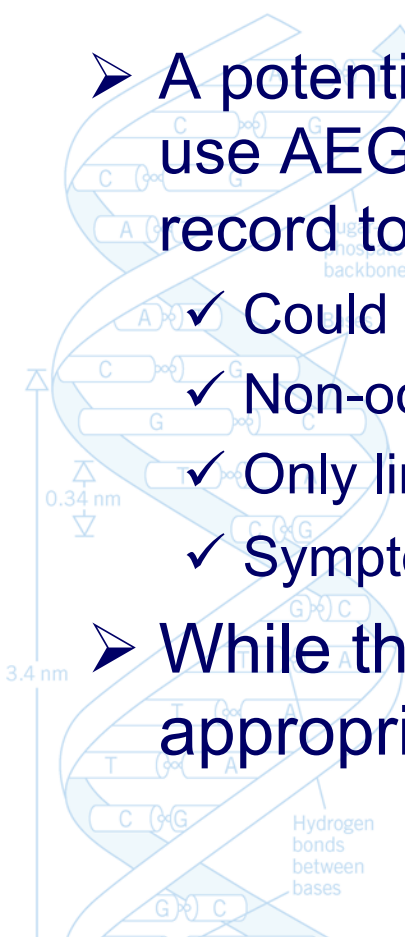
Symptom of infusion related reaction	Symptom experienced?	Most extreme intensity
angioneurotic oedema	yes ☐	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
3.4 arthralgia	yes ☐	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
bronchospasm	yes ☐	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
Other, (specify) _____		mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4

Study Drug administered by infusion

AEs related to Infusion are collected together as a single AE with multiple symptoms

AE of IRR maps simply to the AE domain. Symptoms are not so straightforward

Symptoms of Infusion Related Reactions

- 
- A potential mapping would be to treat each as an AE and use AEGRPID to group all symptoms and the master AE record together
 - ✓ Could be confusing for a reviewer
 - ✓ Non-occurrence of a symptom cannot be mapped
 - ✓ Only limited information is collected about symptoms
 - ✓ Symptoms and AEs would always be analysed separately
 - While this is a valid mapping it was not considered appropriate for this data

Symptoms of Infusion Related Reactions

Infusion related reactions that occur between start of study medication infusion and within 24 hours of the completion of the study medication infusion should be recorded here.

Event: Infusion related reaction **AE.AETERM**

Is this a serious infusion related reaction (see definition in protocol)?

Date of onset
dd mm yy

Time of onset (24 hour clock)
h min

AE.AESTDTC

yes ☐ → complete SAE form within one working day of occurrence and fax immediately to the sponsor
no ☐

AE.AESER

Infusion related reaction

CE.CESEV

Symptom of infusion related reaction	Symptom experienced?	Most extreme intensity
angioneurotic oedema CE.CETERM	yes ☐ CE.CEPRESP = 'Y' CE.CEOCCUR	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
3.4 arthralgia	yes ☐	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
bronchospasm	yes ☐	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4
Other, (specify) _____	CE.CEPRESP = null	mild ☐ CTC grade 1 moderate ☐ CTC grade 2 severe ☐ CTC grade 3 life threatening ☐ CTC grade 4

Mapped to the clinical events (CE) domain

Same structure as AE domain

Allow for the collection of data relating to the non-occurrence of a symptom

Records in RELREC are needed to relate AE records to CE

Smoking History

Smoking history

never smoked ☐

current smoker ☐ → specify number of cigarettes/day if none, enter 0

→ specify number of cigars/day if none, enter 0

→ specify number of pipes/day if none, enter 0

past smoker ☐ → specify time since cessation years months

Data collected once
at screening as part
of baseline
demographics

Additional data
collected depending
on smoking status

Historically this was
mapped alongside
demographic data which is
not appropriate in SDTM

Smoking History

	USUBJID	SUCAT	SUTRT	SUDOSE	SUDOSU
1	AB0123-4567-89012	NEVER SMOKED	TOBACCO	0	CIGARETTES/DAY
2	AB0123-4567-89012	NEVER SMOKED	TOBACCO	0	CIGARS/DAY
3	AB0123-4567-89012	NEVER SMOKED	TOBACCO	0	PIPES/DAY
4	AB0123-4567-34567	CURRENT SMOKER	TOBACCO	24	CIGARETTES/DAY
5	AB0123-4567-34567	CURRENT SMOKER	TOBACCO	0	CIGARS/DAY
6	AB0123-4567-34567	CURRENT SMOKER	TOBACCO	1	PIPES/DAY
7	AB0123-4567-09876	PAST SMOKER	TOBACCO	0	CIGARETTES/DAY
8	AB0123-4567-09876	PAST SMOKER	TOBACCO	0	CIGARS/DAY
9	AB0123-4567-09876	PAST SMOKER	TOBACCO	0	PIPES/DAY

Possible solution is to map all data to SU and SUPPSU

Records are being artificially created where it was not possible to collect data

There is a large amount of data redundancy especially for non-smokers and past smokers

Smoking History

Smoking history

never smoked ☐

SU.SUTRT = 'TOBACCO'

SU.SUPRESP = 'Y'
If > 0 SU.SUOCCUR = 'Y'
If = 0 SU.SUOCCUR = 'N'

current smoker ☐

SU.SUDOSU

SU.SUDOSE

→ specify number of cigarettes/day if none, enter 0

→ specify number of cigars/day if none, enter 0

→ specify number of pipes/day if none, enter 0

past smoker ☐

→ specify time since cessation years months

SC.SCCAT = 'TOBACCO'
SCTESTCD = 'SMKCESS'

SC.SCORRES as an ISO 8601 Duration

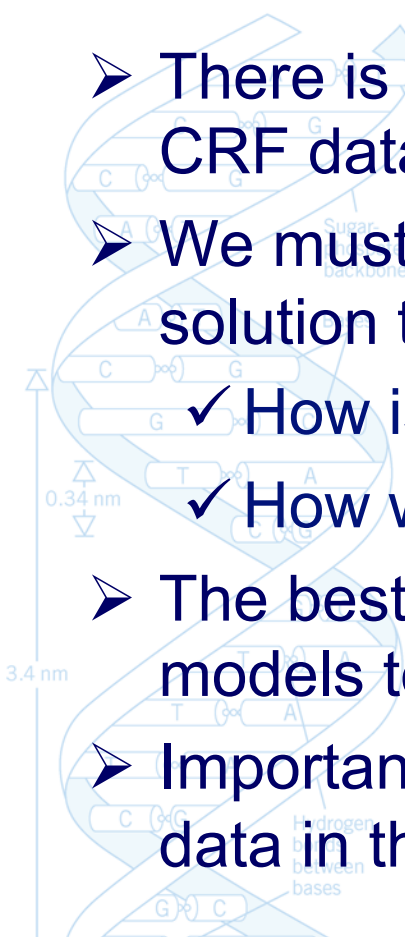
SC.SCCAT = 'TOBACCO'
SCTESTCD = 'SMKHIS'

Smoking history and
time since cessation
both mapped to SC

Amount of cigarettes,
cigars and pipes mapped to
SU

Records in RELREC
are needed to relate
SC records to SU

Conclusion

- 
- There is often no single “correct” approach to mapping CRF data
 - We must consider different factors when deciding which solution to use
 - ✓ How is the data collected and linked
 - ✓ How will the data be analysed
 - The best approach is to create/enhance collection models to map simply to SDTM
 - Important to include those who will map and analyse the data in the definition of the collection model

Questions

