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National Clinical Terminology and Information Service

Adverse Reactions Reference Set Implementation Guide v1.0

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1 Introduction

1.1 Purpose

This document provides a summary of how the Adverse reactions reference set group (the ARRS) and components[1] were developed, as well as more general information about reference set development. There are comprehensive descriptions of the terminology content that the ARRS contains, intended implementation and usage options, and potential considerations for enhancement and expansion.

1.2 Intended audience

This document has been written for those in the SNOMED CT-AU community of practice who are implementing the ARRS or reference sets in general. The document is written for those who have a solid understanding of SNOMED CT[2] and its associated concept model, its scope and underlying description logic.

1.3 Scope

This review does not repeat the extensive development details[3] already provided by NEHTA, but rather focuses on those factors that implementers will need to understand and address in order to deploy the ARRS.

1.4 Related documents

The documents tabulated below provide the context for development of the reference sets described in this document, and should be read in conjunction with this document to enhance understanding of our approach to terminology development. The location of each document within the NEHTA site[4] is provided as well.

Table 1: Related documents

Name	Location
SNOMED CT-AU Development approach for reference sets: [1]	http://www.nehta.gov.au/implementation-resources/ehealth-foundations/snomed-ct-au-common
SNOMED CT-AU Australian Implementation Guidance [2]	http://www.nehta.gov.au/implementation-resources/ehealth-foundations/snomed-ct-au-common

Note: Information on the change history of reference sets is detailed in the *Development approach for reference sets* document.

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[1] The ARRS is a group of reference sets: its components are the *Clinical manifestation reference set*, the *Adverse reaction type reference set*, and the *Adverse reaction agent reference set*.
[2] IHTSDO®, SNOMED® and SNOMED CT® are registered trademarks of the IHTSDO.
[3] See Section 1.4.
[4] http://www.nehta.gov.au/our-work/clinical-terminology.

2 Overview

The ARRS is comprised of three individual reference sets:

- *Clinical manifestation reference set*
- *Adverse reaction type reference set*
- *Adverse reaction agent reference set*

The guidance for implementers of the ARRS provided here is deliberately modest. This reflects the development approaches in constructing the ARRS, and acknowledges that the ARRS is an initial product designed to simplify deployments in the first instance.

Existing components in the ARRS are well constructed, and the terminology content is justified given specified use cases (which primarily related to Detailed Clinical Model binding[5]). Other deployments need to be mindful of these design intentions.

Development approaches have ensured that most terms commonly in use at present are included, and most users will find terminology content that suits their immediate and initial requirements.

SNOMED CT-AU concepts included in these sets have been identified through harvesting existing (legacy) termsets, mapping and clinical review processes. This development approach produces reference sets that are called "extensional reference sets".

Extensional reference sets have inherent limitations, even when well implemented. Concept members have been "cherry-picked" to cover the common concepts used in current practice which makes the overall scale and scope of extensional reference sets appear to be "patchy" with regard to overall SNOMED CT-AU coverage.

These characteristics may influence user expectations of what content should be included, and how users can search for and select the concepts they need to document patient records.

It is expected that some users and implementers will demand more terminology content, as well as perhaps more specificity within that content.

Such demand for additional terminology content to be included in these reference sets, perhaps to satisfy local users and their clinical documentation requirements, introduces the need for implementers to expand on the ARRS content, using other SNOMED CT-AU or AMT concepts.

This document provides advice on how to safely expand the ARRS. Implementers will need to be mindful of how terminology content can be exchanged among health care providers and health data repositories, and interpreted accurately by both senders and receivers.

Reference set maintenance and versioning are also important factors for implementers and users to consider. Updating to new reference set releases will allow deployments to remain current and to ensure that the interchange of terminology content among health care providers and health data repositories is

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[5] "Binding" means the process of aligning terminology content from a reference set with data elements and entry fields in information systems.

supported. Some initial information is provided here to alert implementers to the key factors that they need to consider further.

The guidance provided here is quite general: many implementers will have different opportunities or encounter different obstacles when deploying the ARRS, given their clinical IT systems and operating environments.

Further guidance can be found in the citations and resources referenced in this document.

Additional assistance is available, through NEHTA[6] and the AEHRC[7], however more specific and particular guidance would need to be tailored on a case-by-case basis to suit individual implementers.

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[6] help@nehta.gov.au
[7] enquiries@aehrc.com

3 Development approaches and content

The reference sets were developed collaboratively with contributions of both source vocabularies and clinical guidance from the following organisations:

- Queensland Department of Health
- St Vincent's Hospital Sydney
- ACT Government Health Directorate
- Victoria Department of Health
- Western Australia Department of Health
- Therapeutic Goods Administration (TGA)
- Northern Territory Department of Health
- South Australia Health
- Sydney Adventist Hospital
- Healthshare NSW
- Healthcare Software

Reference sets were developed using the source mapping method followed by clinical review and adjudication.

Existing vocabularies in use, or reference materials, were harvested and these were then mapped or matched to SNOMED CT-AU terminology content. These term listings then were provided to the collaborating stakeholders and NEHTA's clinical unit, who reviewed and advised on the suitability of this terminology content and how well (or not) it met with the identified use cases.

The mapping sources were a combination of different native and legacy vocabularies.

3.1 Scope

As a result of their heritage, these reference sets reflect the terminology content that is already in use by the health information industry. This means that the reference sets are inclusive of concepts that most users are familiar with, but the scope of these reference sets does not exploit all the terminology content that SNOMED CT-AU or AMT has to offer.

Hence, these reference sets are considered to be "starter sets"; expansion of the scope of the terminology may be required in the future to cater for the emerging requirements of users.

3.2 "Patchiness" of content

Because these reference sets were developed from source data, they do not contain all potentially useful content from SNOMED CT-AU or AMT, and as a result the terminology content here may appear to be "patchy". It excludes concepts that users might expect to find. Figure 1 shows a portion of SNOMED CT-AU content relevant to allergic reactions; the green dots represent concepts that are included

in the ARRS. That is, many of the concepts offered by SNOMED CT-AU have been deliberately left out of the ARRS because they:

- did not reflect current terms in use;

- did not meet clinical review acceptability requirements; or

- did not meet use case design requirements for Detailed Clinical Model (DCM) binding.

This is an inherent characteristic of all extensional reference sets, and is not peculiar to the ARRS.

It also highlights the requirement to deploy the whole of SNOMED CT and AMT in clinical information systems to allow users to augment the ARRS content (and overcome the apparent patchiness).
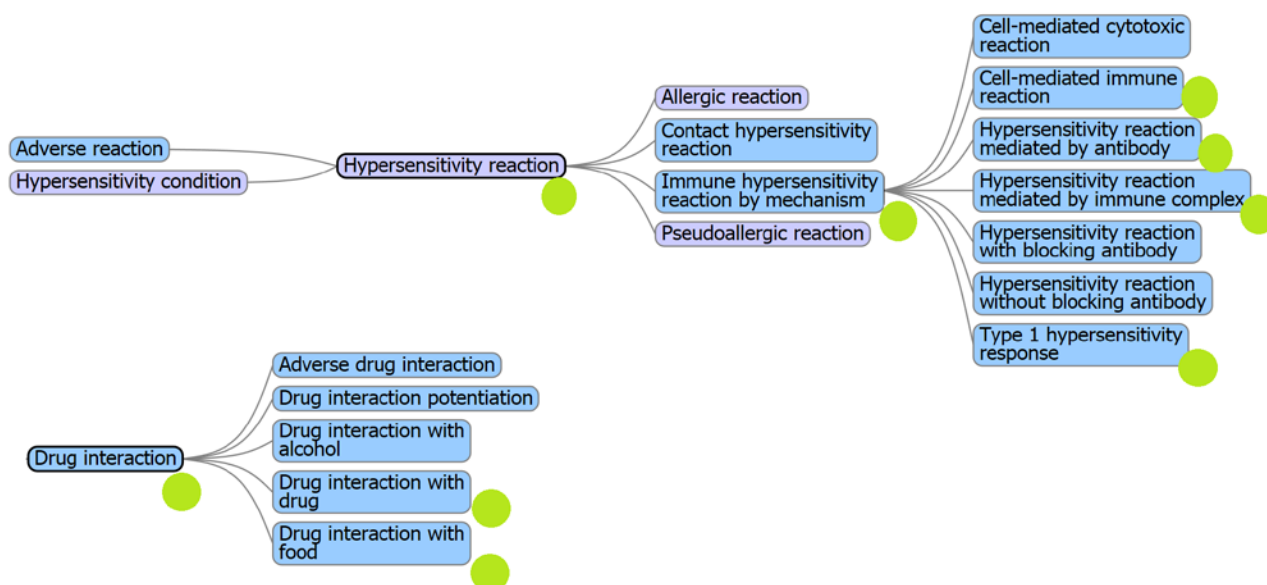
Figure 1: Patchiness in the ARRS (Adverse reaction type reference set)

This patchiness has implications for downstream use of patient data collected using the ARRS. Simple subsumption techniques (using the SNOMED CT-AU Relationships table directly) that might be used to aggregate patient data will not work reliably, and additional manual handling for secondary reporting purposes will be necessary.

3.3   Content characteristics

A number of changes in the *Australian dialect reference set* have been undertaken as part of this reference set work to ensure that usable terms are allocated as the Preferred Term for use in Australia.

The *Clinical manifestation reference set* contains 746 concepts, and there are 3070 associated descriptions.

See Section 4.2 for further information on the use of descriptions.

Table 2: Sample concept members of the Clinical manifestation reference set

SNOMED CT-AU ID	SNOMED CT-AU Fully Specified name
2538008	*Ketosis (disorder)*
2776000	*Delirium (disorder)*
8009008	*Nocturnal enuresis (finding)*
9062008	*Ototoxicity (disorder)*
9748009	*Dyskinesia (finding)*
16539002	*Increased skin sensitivity (finding)*
43005009	*Shuffling gait (finding)*
62507009	*Pins and needles (finding)*
279333002	*Pruritic disorders (disorder)*
288849009	*Unable to breathe (finding)*

The *Adverse reaction type reference set* is shown in Table 3. It has 15 concept members. Content for this reference set was sourced from the *Clinical findings* hierarchy of SNOMED CT-AU.

There are 57 descriptions associated with these 15 concepts.

Table 3: Adverse reaction type reference set

SNOMED CT-AU ID	SNOMED CT-AU Fully Specified Name
7895008	*Drug toxicity*
12263007	*Type 1 hypersensitivity response (disorder)*
28031001	*Cell-mediated immune reaction (disorder)*
33845003	*Idiosyncratic drug effect (disorder)*
59037007	*Drug intolerance (disorder)*
79899007	*Drug interaction (finding)*
83699005	*Hypersensitivity reaction mediated by immune complex (disorder)*
90092004	*Hypersensitivity reaction mediated by antibody (disorder)*
95907004	*Drug interaction with food (finding)*
235719002	*Food intolerance (disorder)*
401207004	*Medication side effects present (finding)*
404204005	*Drug interaction with drug (finding)*
419076005	*Allergic reaction*
421961002	*Hypersensitivity reaction*
609406000	*Pseudoallergic reaction*

The *Adverse reaction agent reference set* contains 1,113 concepts which are associated with 2,839 descriptions, the vast majority of which are drawn from the *Substance* hierarchy in SNOMED CT-AU, with a few exceptions drawn from devices/products for example: 350242003 |*Alcoholic disinfectant (product)*| and 14423008 |*Adhesive bandage (product)*|. The *Substance* hierarchy content has over 23,000 concepts available; the reference set uses slightly less than five per cent of the available terminology content. Examples are shown in Table 4.

Table 4: Sample concepts from the Adverse reaction agent reference set

SNOMED CT-AU ID	SNOMED CT-AU Fully Specified Name
3340007	*alpha-Amylase (substance)*
37663002	*Venom (substance)*
111064005	*Sulfur compound (substance)*
230031005	*Lobster - dietary (substance)*
261277008	*Apricot - dietary (substance)*
373266007	*Anesthetic (substance)*
373498003	*Sunscreen agent (substance)*
387544009	*Floxacillin (substance)*
412068007	*Rye (substance)*
428126001	*Diphtheria vaccine (substance)*

These examples show that reference set membership covers naturally occurring substances (plants, venoms), drug substances (Floxacillin, diphtheria vaccine), chemicals (sulfur compound), manufactured agents (sunscreen), and dietary substances (lobster, apricot).

Some SNOMED CT-AU content has been excluded from this reference set, specifically trade products, brand names of medications, and organisms.

Terminology content in this reference set cannot be used to imply that any agent is associated with an allergy, intolerance or hypersensitivity (pseudo-allergy).

The initial approach in developing this reference set was to standardise terminology content to represent the most common agents causing adverse reactions. Expansion or augmentation of the *Adverse reaction agent reference set* can be achieved by including additional terminology content from other reference sets, such as those in the following table.

Table 5: Terminology content suited for expansion of the ARRS

Reference Set Component ID	Reference Set Name	Source
32570211000036100	*Substance foundation reference set*	SNOMED CT-AU
929360021000036102	*Trade product reference set*	AMT
929360031000036100	*Trade product unit of use reference set*	AMT
929360041000036105	*Trade product pack reference set*	AMT

Reference Set Component ID	Reference Set Name	Source
929360051000036108	*Containered trade product pack reference set*	AMT
929360061000036106	*Medicinal product reference set*	AMT
929360071000036103	*Medicinal product unit of use reference set*	AMT
929360081000036101	*Medicinal product pack reference set*	AMT

4 Advice and guidance

Implementers and vendors need to know a little about the terminology content of the ARRS, but more importantly, they will also need to be mindful of how to deploy the ARRS in their information systems. The way in which the terminology is delivered to clinical users, including characteristics of user-friendliness, search, display, and constraint setting, will influence their understanding, the degree to which they find terminology useful and appropriate, and the acceptability of clinical system performance. These factors are likely to influence clinician behaviour in documenting patient records. There is a difference between the "context of meaning" conveyed by terminology content itself, and the "context of use" of terminology [3], and indeed there are multiple contexts of use.

The advice and guidance provided here outlines key issues that are worthy of further consideration, including aligning terminology content from the ARRS with data elements and entry fields in information systems (referred to as "binding"), search strategies and algorithms, use of synonyms, potential expansion of the ARRS content and maintenance.

4.1 Binding reference sets to information models

The ARRS is intended to be utilised in DCMs, binding terminology content to data elements as shown in Table 6.

Table 6: Reference set binding to Detailed Clinical Models

Reference set and ID	DCM and DE definition	DCM data element number and OID
Adverse reaction agent reference set 142321000036106	*Adverse Reaction DCM* Data element: *Substance/Agent* Identification of a substance, agent, or a class of substance that is considered to be responsible for the adverse reaction.	DE: 15521 OID: 1.2.36.1.2001.1001.101.103.15521
Adverse reaction type reference set 11000036103	*Adverse Reaction DCM* Data element: *Reaction Type* The type of reaction as determined by the clinician.	DE: 15554 OID: 1.2.36.1.2001.1001.101.103.15554
Clinical manifestation reference set 142341000036103	*Adverse Reaction DCM* Data element: *Manifestation* Clinical manifestation of the adverse reaction expressed as a single word, phrase or brief description.	DE: 15564 OID: 1.2.36.1.2001.1001.101.103.15564

Although specified as DCM and value sets, these reference sets can be utilised in other data elements in clinical systems that do not utilise DCM specifications[8].

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[8] As with many other NEHTA-developed reference sets, the *SNOMED CT-AU Development Approach* [1] notes that "This reference set may be applicable for use cases outside of this specification".

These reference sets have been developed for primary use cases, to enable capture of clinical information at the point of care, in individual health records. However, other downstream data requirements are also known, specifically, monitoring of adverse drug events by the TGA in the Database of Adverse Event Notifications collection [4] [5][9].

4.1.1 Data elements or fields in the clinical information system

The design and construction of the ARRS necessarily takes a DCM approach. Detailed Clinical Models are a basic minimum standard specification of an information model; these are somewhat generic in their specification.

Comprehensive information about the specification of DCMs is available in the *Adverse reaction DCM specification* [6].

Information about the intended use of the DCM and terminology components, UML diagrams, data elements and data hierarchy is provided. Known issues and limitations, and potential misuse warnings are also outlined here.

It is acknowledged that not all implementers or clinical system vendors have software implementations that exactly reflect these DCMs. However it should be noted that considerable clinical guidance has helped to frame these specifications, and most users will find some generic and re-usable artefacts that can be tailored to suit their own purposes, closely mimicking these DCM approaches.

Because the ARRS has been focussed on DCM specifications, it would seem that some terminology content has been excluded so as to not impede the collection of other data, such as anatomy or causal mechanisms.

This is illustrated by the clinical decision criteria applied to terminology content in the *Clinical manifestation reference set*.

The key exclusion criteria were:

- Concepts shall not contain more than one manifestation type unless considered clinically relevant.

- Concepts shall be void of causative agent information.

- Concepts shall be void of severity information.

- Concepts not attributable to an adverse reaction shall be excluded.

- Concepts that exist in combination with body sites shall be excluded unless considered clinically relevant.

By excluding content with these characteristics, the ARRS allows implementers to capture information about anatomical structures and causal mechanisms in distinct and separate data elements. For example (see Figure 2 below) 449671007 |*Cellulitis of upper limb*| is not included in the ARRS. This allows users to search for and select a more general term of 128045006 |*Cellulitis*| (included in the ARRS) and then separately search for and select whichever anatomical structure is affected for the patient (upper limb, skin, head, neck or digit). These anatomical structure concepts would be drawn from 32570061000036105 |*Body structure foundation reference set*|.

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[9] Use of the ARRS for secondary reporting will be addressed in subsequent guidance documents.

This approach is analogous to close-to-user post coordination, and allows users to precisely document the conditions that the patient experiences, without requiring SNOMED CT-AU to provide a pre-coordinated term for every anatomical structure and every reaction. This would otherwise lead to combinatorial explosion, and a massive increase in the size of the terminology. Avoiding combinatorial explosion is a considerable advantage.

But this approach relies on the information system providing a data element specifically dedicated to the collection of anatomical structures, and would also require the information system to bind the 32570061000036105 |*Body structure foundation reference set*| to that data element.

Close-to-user post-coordination techniques are entirely suitable, if the clinical information system provides all the required data entry fields. However, this approach brings some disadvantages also:

- It introduces the need for users to search for and select multiple concepts to accurately document the patient condition.

- It creates additional steps in the clinical documentation workflow, with the potential for incomplete data.

- There is the possibility of erroneous data being captured that might introduce conflicts.

Concepts such as *Cellulitis of upper limb*, that are fully defined, already carry this anatomical information with them, by virtue of their definition in SNOMED CT-AU. Here we see that the finding site is already specified (see Figure 2).

Using the defined relationships within SNOMED CT-AU would allow a clinical information system to auto-populate a separate body site, without requiring users to separately search, select and enter this information.
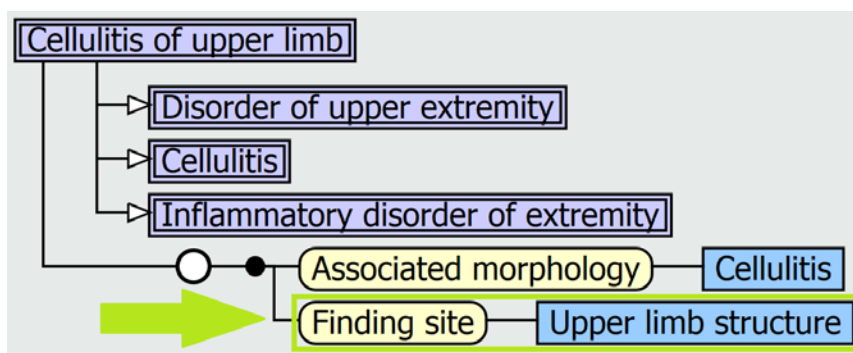
Figure 2: Use SNOMED CT-AU defining relationships to auto-populate data elements

If the clinical information system that will deploy the ARRS is configured differently from DCM specifications, then other options for binding may be more suitable.

It will be necessary for implementers to tailor the ARRS content to:

- suit the clinical information system and configuration that will deliver this terminology content;

- reduce the number of fields that clinical users will have to complete;

- reduce the number of searches, keystrokes or mouse clicks it takes to complete a patient record; and to

- minimise the possibility of erroneous or conflicted concept entries.

4.1.2   Reference set use in CDA messages

NEHTA documentation also provides guidance for representing terminology in CDA messages in *Representing Coding in CDA Documents: Implementation Guidance* [7].

Section 2.1.6 of this document explains that:

> *"…data elements may have a value set assigned, which specifies the set of allowed values for the codes. Simple value sets specify a list of possible codes… In the context of NEHTA specifications, when value sets are assigned, they are always simple lists of codes taken from a single code system. Most of the NEHTA specified value sets – especially the clinical ones – are taken from SNOMED CT-AU or AMT. In these cases, the value sets are simple lists of possible codes defined as SNOMED CT-AU reference sets, and included in the SNOMED CT-AU and AMT releases."*

This guidance goes on to say:

> *"Because all the value sets are based on a single coding system, this document refers to an expected code system or an expected value set interchangeably. Because CDA doesn't directly reference the value set, but does reference the code system directly, the document focuses on expected code systems."*

This is an extremely important distinction.

That is, the specification of dedicated value sets, with distinct OIDs, bound to distinct DCMs (or CDA data elements) implies that these encoded concepts are the only and expected allowable values that will be required by, used by, sent or received in messages or documents exchanged by clinical users and implementers.

Any expansion of the ARRS to include concepts that are **not** included in these reference sets (as released) may not be validated by receiving systems.

4.2   Search and selection

4.2.1   Use of descriptions

Descriptions or synonyms in SNOMED CT-AU aid search strategies. They provide alternate lexical representations of a concept, and share the same meaning. This means that there are different terms available for users, who may have their own preferred abbreviations or acronyms that they routinely use to document patient cases; they do not have to know or remember how SNOMED CT-AU describes conditions, nor do they have to change the way they prefer to describe patient conditions. An example is shown in Figure 3, where we see that the concept 42343007 |*Congestive heart failure*| can also be described as "CHF", "CCF", "Congestive cardiac failure" or "Congestive heart disease". It doesn't matter whether different users describe conditions using different words; synonyms help to ensure that all users understand the precise, unambiguous meaning by referring to the concept.

PROPERTY	VALUE
SCTID	42343007
Primitive	true
Active	true
Effective Time	20020131
Module Id	900000000000207008
FSN	Congestive heart failure (disorder)
Synonyms	Congestive cardiac failure
	CHF - Congestive heart failure
	Congestive heart disease
	CCF - Congestive cardiac failure
	Congestive heart failure

Figure 3: Use synonyms to aid search and selection

4.2.2   Record descriptions and concepts

Despite that fact that using synonyms provides search advantages, it should be noted that the word representations of synonyms are not unique. Description IDs are unique, but users generally don't have visibility of descriptions or concept IDs, so they will not be able to differentiate between the same words that have different meanings.

Figure 4 shows an example of this in SNOMED CT-AU. We see that the words denoting Pyogenic arthritis are associated with three different and distinct concepts, and therefore have three different and distinct meanings. This is called semantic drift.

PROPERTY	VALUE
SCTID	372940009
Primitive	false
Active	true
Effective Time	20020731
Module Id	900000000000207008
FSN	Acute suppurative arthritis (disorder)
Synonyms	Acute suppurative arthritis
	Pyogenic arthritis

PROPERTY	VALUE
SCTID	372939007
Primitive	false
Active	true
Effective Time	20020731
Module Id	900000000000207008
FSN	Suppurative arthritis (disorder)
Synonyms	Septic arthritis
	Suppurative arthritis
	Pyogenic arthritis
	Pyoarthrosis

PROPERTY	VALUE
SCTID	48245008
Primitive	false
Active	true
Effective Time	20020131
Module Id	900000000000207008
FSN	Bacterial arthritis (disorder)
Synonyms	Arthritis due to bacterial infection
	Septic arthritis
	Pyogenic arthritis
	Bacterial arthritis
	Arthropathy associated with bacterial disease

Figure 4: Semantic drift, synonyms related to different concepts

For this reason it is necessary that deployments of the ARRS, as well as SNOMED CT-AU and AMT generally, have the following capacities:

- Search strategies should exploit descriptions (synonyms).

- Displaying the preferred term of the concept associated with descriptions to the user.

- Capturing the term selected (descriptions) by the clinical users.

- Capturing the associated concept as well, for unambiguous documentation.

4.2.3 Recognition not recall

The most generic guidance for developing terminology search strategies for clinical information systems is to favour recognition not recall. That is, the functionality provided must support clinical workflows, and users should:

- not have to remember terms;

- not have to "know" how SNOMED CT-AU or AMT represents the words; and

- be able to quickly find and visually identify the terms they need easily.

Search strategies that force users to recall their favourite or easily findable terms will have the effect of biasing patient data collections; users will continually use their "favourite" terms rather than the full complement of terms available, which might be more precise, specific and better suited to unambiguous clinical documentation. Recall strategies mimic the use of cheat sheets or crib sheets, and blunt the descriptiveness of clinical documentation.

4.2.4 Search algorithms

Implementers of clinical information systems should consider the following recommendations:

- Index the terminology – stop words such as "no" "not" "without" need special handling; terms such Vitamin A will be ignored if the letter "A" is included as a stop word.

- Use key word alternates (nose=nasal; renal-kidney).

- As a minimum, use "starts with", "any order" for example: allow prefix matching (such that entering "emer lap app" will return "emergency laparoscopic appendectomy").

- Consider fuzzy searches and phonetic matching.[10]

- Provide progressive matching as the user types in text (autocomplete).

- Match text against SNOMED CT-AU concept preferred term and synonym descriptions.

- Employ a statistical word matching algorithm such as those available in Lucene.

- Communicate to the user where a match is a synonym.

- Allow the user to confirm the suggested matches before they are saved.

These brief points are not exhaustive and merely summarise some of the important considerations for implementers who are designing and building clinical information systems that will deliver SNOMED CT-AU and AMT content. Extensive guidance and

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[10] This is often referred to generically as "soundex". However, soundex is a specific algorithm which does not perform particularly well when compared to modern approaches.

examples[11] are provided for SNOMED CT-AU generally [8] and for recording adverse reactions in particular [9].

Clear guidance is provided in these documents, with numerous explanations of intent and purpose, and helpful screen renditions. But the most valuable recommendations for implementers will be about "what not to do".

This guidance is well regarded internationally, and serves as a recommended Common User Interface (CUI) design for health information systems. The advice is somewhat generic so that it can be adapted and applied to different clinical system architectures and requirements.

It is acknowledged that different systems will employ different screen displays, use different widgets, have different workflows and functionality for users.

Advice here focuses on the fundamentals of terminology delivery to users, and is regarded as non-negotiable. Some of the features and functionality recommended here will be essential for conformance and compliance assessment of clinical information systems.

4.2.5   Structured forms

Many existing clinical information systems use structured forms, where users "fill in" various data entry boxes and navigate through in order to comprehensively document a patient record.

Software designers will need to be aware of the height and length data entry fields to avoid truncating or hiding terms with long descriptions.

The design and use of screen real estate, intuitive layout, and visibility, are all important considerations. Considerable research on usability issues offers invaluable guidance [10] [11] [12] [13] but is not duplicated in this document.

Keep in mind the sort of behaviour and actions that users will perform, particularly the data entry techniques such as typing, mouse-clicks and scrolling. Mixed methods add to data entry effort.

4.2.5.1   Drop down lists

As a general rule, drop down lists should only be used when there are a small number of relevant terms to be viewed and selected. Long lists presented to users will force them to scroll and navigate in order to identify the term they need. Long lists of terms also consume a lot of screen real estate. If the search return list has more than 20 terms, then implementers should consider phasing the presentation of search results and allowing the user to expand or click through to see the terms displayed in position 21 or greater.

A drop down list might be suitable for the *Adverse reaction type reference set* content provided by the ARRS, but be wary of how many concepts might be displayed if this reference set is expanded.

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[11] Common User Interface (CUI) guideline documents pertaining to SNOMED CT or terminology coding are available on http://www.mscui.net [20] or http://www.cui.nhs.uk [19] (free user registration required).

4.2.5.2   Radio buttons

If the data entry options are dichotomous (such as yes, no; absent, present) or there are less than six terms (such as male, female, indeterminate) then radio buttons may be a reasonable user interface option. All terms presented should be mutually exclusive.

4.2.5.3   Check boxes

Check boxes are also a useful interface data entry option, but choices must be independent, and consideration needs to be given to whether multiple boxes can be validly checked so all relevant terms can be recorded. Generally, check boxes work best when data entry terms number less than 10.

4.3   Expansion of reference sets

Expansion techniques are not always as easy as introducing a secondary search strategy, and some expansion techniques may be beyond the expertise of local users or vendors, especially if they do not have access to specific clinical or terminology expertise, or tools tailored to their requirements.

Caution is needed when expanding the ARRS reference sets so that Grouper reference set members are not unintentionally referenced. The consistency between intensional (inclusional) reference sets and exclusion reference sets, such as the *Grouper reference set* and the *Non-human reference set*, as well as preferences for *Australian dialect reference set* need to be taken into account.

4.3.1   Use the ARRS out of the box — a constrained value set only

Reference sets are sometimes wrongly regarded as stand-alone value sets, an exhaustive, exclusive, enumerated list of allowable code values (only). This is one way of regarding and using reference sets, but other options may be more benficial.

Using reference sets in this way constrains clinical users, only ever allowing them to search, view, select and enter concepts from within these reference sets.

If the particular concept a clinical user needs or wants is not present as a member of this set, then they would have to revert to narrative entries in the document.

There are a number of disadvantages to this approach:

- The use of a small, hand-picked set of SNOMED CT-AU or AMT concepts, which reflect existing (legacy) terms, does not exploit the richness or currency of terminology on offer in the entire corpus of SNOMED CT-AU or the AMT.

- Text entries are generally not (easily) amenable to computation and are unsuited for all consolidated summaries and reporting purposes.

- The patchiness evident within these extensional reference sets may well frustrate clinical users who might demand more or different concepts to populate patient records accurately.

Reference sets are not necessarily regarded as absolute constraints on terminology content. They are merely those agreed and prioritised concept members in a set derived from the whole code set, in this case SNOMED CT-AU and AMT.

Key points to note include:

- Sanctioned lists are not the only way to employ reference sets.
- Domain reference sets can be used to improve the user selection/search experience.
- Broad context reference sets generally do not suffer from the limitations given above.

4.3.2 Expanding? Then consider Postel's law, the robustness principle

The fundamentals of exchange of health information, point-to-point and point-to-store, are founded on the ability of everyone to send, receive, understand and interpret clinical information accurately and as intended. This requires a level of co-operation, acceptance of standards and conformance and compliance.

It also requires that everyone implement the entire codes system, not just the reference set.

These principles are encapsulated in Postel's Law, and various responses to the robustness principle outlined here: [12]

Jon Postel's legacy includes a Robustness Principle which is often labeled Postel's Law: "an implementation should be conservative in its sending behaviour, and liberal in its receiving behaviour" (reworded in RFC 1122 as "Be liberal in what you accept, and conservative in what you send").

This presupposes using the entire code system, SNOMED CT-AU and AMT; that is the deployment of the whole of SNOMED CT-AU or AMT is a prerequisite for using reference sets.

This prerequisite ensures that all users can send the ARRS terms, but that everyone can also receive and correctly interpret any other SNOMED CT-AU or AMT concept.

It may indicate that implementers will need to employ a terminology server capable of properly delivering both SNOMED CT-AU and AMT content.

Reference sets might be regarded as "pref erence sets" of terminology content.

Reference sets provide a list of concepts that are preferred and recommended, by design and clinical guidance, for first line use in clinical systems.

There are some options to expand the content of the ARRS to satisfy the broadest possible demand and use of terminology content in myriad clinical settings. These include:

- Request additional content by contacting help@nehta.gov.au.
- Pre-compute the expanded content:
  - 2nd line strategy: careful expansion in compliance with original ARRS design principles.
  - 3rd line strategy: include only child or descendant concepts of existing ARRS concepts.
- On-the fly expansion by users through search strategies.

These options are explored further below.

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[12] http://en.wikipedia.org/wiki/Robustness_principle.

4.3.3   Compliance with design principles, 2nd line strategy

Replicating the design and editorial criteria for reference set expansion, in order that an expanded reference set remain faithful and interoperable with the ARRS release content, can be difficult for users, and indeed in some instances for terminology developers and analysts.

The editorial and acceptance criteria for the *Clinical manifestation reference set* (for example) states that:

1   Concepts shall not contain more than one manifestation type unless considered clinically relevant.

2   Concepts shall be void of causative agent information.

3   Concepts shall be void of severity information.

4   Concepts not attributable to an adverse reaction shall be excluded.

5   Concepts that exist in combination with body sites shall be excluded unless considered clinically relevant.

If users are inclined to expand the *Clinical manifestation reference set* to suit their own implementation and user requirements, then points 2 and 3 of these exclusion criteria can be replicated with existing approaches to query language, for example additional (candidate reference set) members could be identified by a query such as:

```
Let
 candidates = DescendantsAndSelf(404684003 |Clinical finding|),
 sites = HasRels( 363698007 | Finding site | = All ),
 manifestations = HasRels( 363705008 = All ),
 causatives = HasRels( 246075003 |Causative agent| = All ),
 severities = HasRels( 246112005 |Severity| = All )
In
 Exclude( candidates, Union( causatives, severities, sites, manifestations ) )
```

This is a reasonable 2nd line expansion strategy that would reflect some, but not all, of the editorial criteria that framed the development of the ARRS.

It will be noted that the above code fragment will produce a maximal set of concepts that should be excluded from an expanded set, because this query identifies "out of scope" concepts that have relationship types of causative agent and severity (points 2 and 3 of the editorial and acceptance criteria).

However, local users and implementers will not necessarily make the same clinical judgments as outlined in points 1, 4 and 5 of the editorial and acceptance criteria. Different judgements will result in different reference set membership. That is, original editorial judgements are opaque to users, not explicitly knowable, and cannot be replicated in a standard fashion among different developers, different systems, and users.

This is not a criticism of the ARRS.

Extensional reference sets will not be reproducible, and will be difficult to maintain and standardise if they are based on:

- legacy data (or mapsets);
- hand-crafting techniques (pick and choose);
- inclusion criteria that are not "queryable"; or

- decisions made by individual (clinical or terminological) advisors, at a point in time.

4.3.4   Inheritance and subsumption, 3rd line strategy

SNOMED CT-AU and AMT are arranged in a hierarchical structure where specific subtype concepts are defined by an IS A relationship referring to the more general concept. Sometimes these relationships are called parent-child, where the child concepts (subtypes) "inherit" definitional characteristics from their immediate parent. Conversely, we can say that parents "subsume" child concepts. In Figure 5, we would say that *Cellulitis* is a parent, the concepts contained in the light blue shaded box are child concepts and the concepts contained in the lilac shaded box are descendants (or grandchildren).

Child and grandchild concepts shown here are not included in the *Clinical manifestation reference set*, but the parent concept, *Cellulitis*, is an ARRS member.
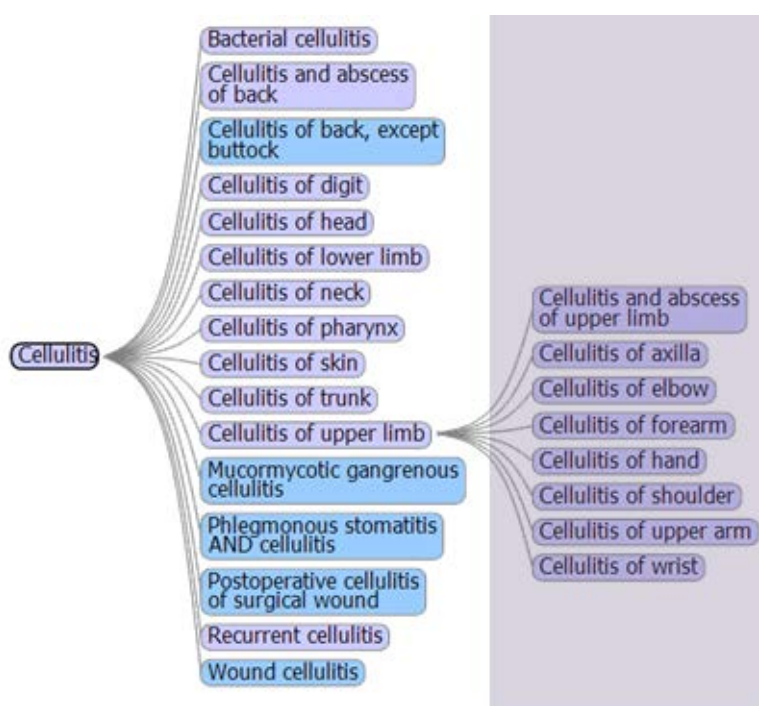

Figure 5: IS A hierarchy and subsumption options

The hierarchical structure provides another way of expanding the ARRS content. Implementers might prefer to meet clinician requirements for increased specificity by including concepts such as *Cellulitis of upper limb*. This is a direct child of *Cellulitis*, so traversing the IS A relationships, this concept could be "rolled" up to its proximal parent, and recorded as "*Cellulitis*" if a more general ARRS concept member was required for exchange or reporting purposes.

However, even more specific terms (descendant or grandchild) like *Cellulitis of shoulder* do not have a direct proximal parent that is a member of the ARRS – the ARRS member *Cellulitis* is "once removed" and unreachable through a direct IS A relationship, because the intervening concept (*Cellulitis of upper limb*) is not present. This is a function of (i) the editorial and design criteria of the ARRS, and (ii) the resultant patchiness.

Three recommendations can be made:

1 Subsumption techniques for expansion purposes need to be performed on the whole of SNOMED CT-AU or AMT, not just reference set content.

2 Subsumption techniques may be necessary if the terminology content contained in in-bound messages has been expanded in a broader, different or more liberal manner than the receiving system has available.

3 Transitive closure techniques provide an alternate path that transits through (or skips over) non-ARRS members and provides traceability to a parent or grandparent concept that is a member of the ARRS.

4.3.5   On-the-fly expansion of terminology content

The use of a properly configured terminology server could present users with the ability to expand terminology on-the-fly, while completing a patient record. A terminology server could be used to present – or boost – concepts in an increasing order such that:

- ARRS members are a first line search return, preferentially favouring initial and agreed content.

- Any pre-computed expanded content (mimicking ARRS editorial or design criteria) is indexed and prioritised as a 2nd phase return.

- Any pre-computed expanded content (based on subsumption or transitive closure results) is indexed and prioritised as a 3rd phase search return.

- Finally, expansion to a more liberal constraint (such as the *Clinical finding foundation reference set* or the *Substance foundation reference set*).

Any expansion techniques need to carefully **exclude** terminology content that is contained in the *Non-human reference set* and *Grouper reference set* and to be aware that the *Australian Dialect Reference Set* nominates different display names as preferred terms for use in Australian context.

4.3.6   Potential clashes between SNOMED CT-AU and AMT content

The initial approach in developing this reference set was to standardise terminology content to represent the most common agents causing adverse reactions; it is well documented that this reference set is not exhaustive.

Recommendations for the expansion or augmentation of the *Adverse reaction agent reference set* can be achieved by including additional terminology content from other reference sets, including those in the following table.

Table 7: Terminology content suited for expansion of the ARRS – Agents

Reference Set Component ID	Reference Set Name	Source
32570211000036100	*Substance foundation reference set*	SNOMED CT-AU
929360021000036102	*Trade product reference set*	AMT
929360031000036100	*Trade product unit of use reference set*	AMT
929360041000036105	*Trade product pack reference set*	AMT
929360051000036108	*Containered trade product pack reference set*	AMT

929360061000036106	*Medicinal product reference set*	AMT
929360071000036103	*Medicinal product unit of use reference set*	AMT
929360081000036101	*Medicinal product pack reference set*	AMT

However, some caution is needed when expanding the *Adverse reaction agent reference set*, given that both SNOMED CT-AU and AMT contain concepts that are potentially equivalent. The two tables below provide examples where potential differences might become evident if different users expand this reference set using different options.

Table 8: Explicitly handle all potentially "expanded" content – example 1

Concept ID	Concept name	Drawn from		
387458008	aspirin	32570211000036100	*Substance foundation reference set*	SNOMED CT-AU
21719011000036107	aspirin	929360061000036106	*Medicinal product reference set*	AMT
925552011000036105	Aspirin (Mayne Pharma)	929360021000036102	*Trade product reference set*	AMT

Table 9: Explicitly handle all potentially "expanded" content – example 2

Concept ID	Concept name	Drawn from		
387517004	Acetaminophen	32570211000036100	*Substance foundation reference set*	SNOMED CT-AU
21433011000036107	paracetamol	929360061000036106	*Medicinal product reference set*	AMT
53173011000036109	Paracetamol (Nyal)	929360021000036102	*Trade product reference set*	AMT

Any of these concepts could conceivably be listed in a legitimate and conformant clinical document.

In order to be "liberal in what you accept", systems need to deploy the entire corpus of SNOMED CT-AU and the AMT, and perhaps even the SNOMED CT-AU to AMT substance mapping table.

Software needs to be explicitly designed to handle all reference sets that can potentially be used to expand the ARRS's agents.

4.3.7 Dealing with out-of-specification terminology content

Any terms that are developed locally, perhaps reflecting specific clinician, geographic or colloquial preferences (such as "acopia" for inability to cope) are regarded as out-of-specification terminology content. This applies also to any non-

formal description used in patient records such as "frequent flyer" (for drug seeking behaviour) or acronyms such as "JNR" (for just not right).

Local extensions, even if formal and authored in compliance with SNOMED CT-AU and AMT editorial specifications, are also regarded as out-of-specification for interoperability purposes, as there is no guarantee that these will be available to all users.

Additionally, proprietary terminologies should be treated with caution, as it is known that most are not mandated standard terminologies, they are not cheaply or readily available, nor are they licensed by the majority of users and deployments.

The majority of termsets that are currently available in vendor software products (legacy termsets) have been developed to suit the customers of that software in particular, and these termsets are generally not shared or shareable with other users. Any termset content that is specific to a software product should not be included in SNOMED CT-AU or AMT deployments.

If implementations do insist on locally developed terms, these could be mapped to formal SNOMED CT-AU or AMT representations. Mapping remains the obligation of local developers as only they can properly know the precise meaning of the local, original term, and its intended use.

From an interoperability perspective it is safest to not expand the ARRS to implement and use terminology content that the broad community will not also have access to. Nor is it safe to create local content (local terminology extensions) that the broader community will not have access to.

If such content is contained in in-bound messages, then receivers will either have to reject the message or undertake manual handling to accurately interpret the intended meaning.

4.4 Useful terminology management techniques

4.4.1 Transitive closure

Transitive closure techniques are outlined in the *SNOMED CT Technical Implementation Guide* [14][13], along with SQL code fragments. These are likely to be useful to implementers in order to:

- Find candidate terminology content suited to expanding the ARRS.

- Find and understand the relationships and meaning of terminology content in in-bound messages (that receivers may not have deployed).

- Find all terminology content that is related to a drug class to assist with decision support queries (for example, find all descendants of 373247007 |*Cardiovascular agent*|).

Transitive closure is expensive in terms of size; a pre-computed transitive closure table usually contains approximately 30 million rows of data, and introduces what might be regarded, from a user perspective, as redundant relationships. The *SNOMED CT Technical Implementation Guide* [14] states that transitive closure is recommended for use in any environment requiring high performance where disk capacity for storage and/or bandwidth for distribution are not a problem.

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[13] Section 7.7.5.2 "Transitive Closure Implementation" also includes code for producing a transitive closure table.

Figure 6 shows the differences. The upper panel shows immediate subsumption relationships. The lower panel shows transitive closure, where the orange lines are (inferred) relationships that reach all ancestors. Note that subsumption proceeds "one step at a time" and traverses only the IS A relationships as distributed.
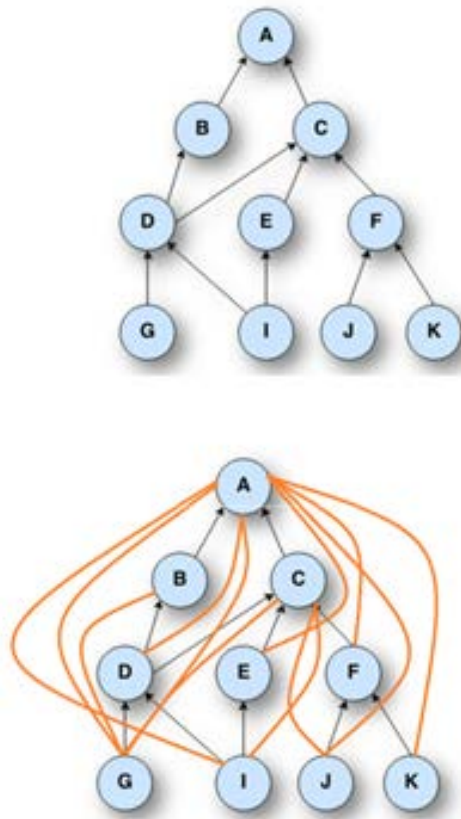

Figure 6: Subsumption and transitive closure

Note that the transitive closure technique "connects everything to everything" without having to traverse step-wise through each concept. All concepts are traceable and reachable using transitive closure.

Further information and assistance can be found on the IHTSDO website, and in toolkits and documents tabulated below.

Table 10: Transitive closure resources

Name	Location
IHTSDO Transitive Closure Library [15]	https://github.com/IHTSDO/snomed-publish/tree/master/lib/closure
IHTSDO Glossary [16]	http://ihtsdo.org/fileadmin/user_upload/doc/en_us/gl.html
SNOMED CT Technical Implementation Guide [14] Section 5.5.3.5 "Transitive Closure History File"	http://ihtsdo.org/fileadmin/user_upload/doc/en_us/tig.html?t=trg2main_format_tchistory
UK Terminology Centre TRUD downloads [17]	https://isd.hscic.gov.uk/trud3/user/guest/group/2/pack/7

4.5 Maintenance

4.5.1 Release cycles

SNOMED CT-AU is updated regularly, and a new version is released every six months (May and November). Each new release of SNOMED CT-AU includes updated or additional reference sets. This release cycle is deliberate so that the terminology remains clinically current, and ensures that continuous quality improvements to terminology content are made available to users as soon as possible.

AMT is released every month. This release cycle serves medication safety requirements, incorporating new drugs that have come to market through regulatory authorities, and reflecting any changes (revisions or enhancements) to the terminology.

Licensing conditions oblige users to keep up to date with new versions.

4.5.2 Changes to terminology content, dealing with historical data

Terminology concepts may be active in one version, and inactive in the next version. They may be inactivated in order to be replaced with a new, more precise (less ambiguous) concept, or to improve quality (text representation to aid human readability or understanding), the definition might have changed, or they may have been inactivated because they were erroneous or duplicated other terminology content.

These inactivated concepts persist (they are not deleted), but:

- they are no longer available for data entry in deployed systems using current versions; or

- they will appear in patient data collected in deployments that delivered previous versions of the terminology (where they were current and active) were deployed.

Recommendations for dealing with new versions include:

- Update terminology versions regularly.

- Inbound data should be handled by clear protocols that include exception handling for inactive content.

- Build system resilience so that it can handle inactive concepts in historical patient data collections.

Far more comprehensive advice for dealing with versions, releases, content change and the potential impacts on systems and deployments is available [18]. This guidance is thorough and although tailored to the UK operating environment, the issues and options it explores are equally valid for all SNOMED CT and AMT implementers.

5 Summary recommendations

The guidance provided here refers to, but does not adequately replace, the technical specifications and guidelines provided by more comprehensive publications. These have been cited in footnotes and formal references throughout this document.

It is recommended that implementers carefully review the available documentation and adapt the advice to their own operational context.

However, there are some key recommendations that should be commonly observed by all implementers to support interoperability and exchange.

5.1 System resilience

- Build system resilience to that it can handle inactive concepts in historical patient data collections.
- Update terminology versions regularly.
- Inbound data should be handled by clear protocols that include exception handling for inactive or out-of-scope content.

5.2 Context of deployment

Observe deployment requirements: if the ARRS is being used in DCM and CDA, do not expand the reference set for use in local installations, nor should local extensions of content be developed and included in the reference set. Depending on the operational context, implementers may:

- restrict data capture to the ARRS only (active ONLY) (DE-15564); or
- treat anything not in (active OR inactive) the *Clinical finding foundation reference set* or the *Problem/diagnosis reference set* as invalid (DE-15564).

5.3 Expansion techniques

- Be careful to observe *Australian dialect reference set* preferred terms.
- Expansion techniques should **exclude** content contained in the *Clinical finding grouper exclusion reference set*.

5.4 Search and select approaches

- Favour recognition **not** recall as search and usability strategies.
- Display the preferred term of the concept associated with descriptions to the user.
- Capture the associated concept as well as the description to enable unambiguous documentation.

Acronyms

Acronym	Description
AMT	Australian Medicines Terminology
ARRS	Adverse reactions reference set group
CUI	Common User Interface
DCM	Detailed Clinical Model
DE	Data element
OID	Object identifier
SNOMED CT	Systematized Nomenclature of Medicine, Clinical Terms
TGA	Therapeutic Goods Administration
UML	Unified Modeling Language

Glossary

Term	Meaning
Binding	The process of aligning terminology content from a reference set with data elements and entry fields in information systems.

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