

TS does not mean T(o) S(uffer) - A hands-on guideline for a better understanding of the TS domain

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At Clinipace, it's personal.

▶ Goal of Paper:

- ▶ Explain purpose and structure of TS domain
- ▶ Provide place for pooled sources of TS information
- ▶ Provide information and personal strategy for challenging parameters of the TS domain
 - ➔ content of this presentation

- ▶ The views and opinions expressed in this presentation are those of the author and do not necessarily reflect the official positions of the FDA, CDISC or any other mentioned organization.

Agenda

1. TSPARMCD = SPONSOR (Clinical Study Sponsor)
2. TSPARMCD = INDIC (Trial Disease/Condition Indication)
3. TSPARMCD = TDIGRP (Diagnosis Group)
4. TSPARMCD = TRT (Investigational Therapy or Treatment)
5. TSPARMCD = PCLAS (Pharmacologic Class)

1. TSPARMCD = SPONSOR (Clinical Study Sponsor) → **dun&bradstreet**
2. TSPARMCD = INDIC (Trial Disease/Condition Indication) → **SNOMED CT**
3. TSPARMCD = TDIGRP (Diagnosis Group) → **SNOMED CT**
4. TSPARMCD = TRT (Investigational Therapy or Treatment) → **UNII**
5. TSPARMCD = PCLAS (Pharmacologic Class) → **MED-RT**

TSPARMCD = SPONSOR

- ▶ Provides name of the responsible clinical trial sponsor and their registered DUNS (Data Universal Numbering System) number
- ▶ DUNS number is provided by dun&bradstreet and can be identified by:
 - using the UPIK[®]-Search function on the UPIK[®] portal („developed by the German Association of the Automotive Industry and the German Chemical Industry Association in cooperation with Bisnode D&B Deutschland“
 - using the search function on the dun&bradstreet website (theoretically)

TSPARMCD = SPONSOR

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 **UPIK® – Unique Partner Identification Key**

MEMBER OF
dun & bradstreet
WORLDWIDE NETWORK

[Home](#) | [Bisnode D&B Germany](#) | [D&B International](#) | [VDA](#) | [VCI](#) | [Contact](#) | [Login](#)



D&B D-U-N-S® NUMMER

UPIK®-Search with D-U-N-S® number

UPIK®-Search with name

D-U-N-S® Number Request

eUpdate

My UPIK®

UPIK® Knowledge Base



[Industry Report Automotive](#)

► Home ► Suchen

UPIK®-Search

Access information about **257.121.323** companies worldwide – instantly and cost-free. Thanks to the D&B D-U-N-S® Number, all companies are clearly identified and associated data are correctly classified.

If you don't know the D&B D-U-N-S® Number of the company you're seeking, please enter the name and address of the company into the fields below.

Company *

Address

Zip Code

City

Country *

☐ Ich bin kein Roboter.


reCAPTCHA
Datenschutzerklärung - Nutzungsbedingungen

Find

My UPIK® - Login

Username:

Password:

[Forgotten your password?](#)

[Register now](#)

More on the topic

[How does the UPIK®-Search work?](#)

[When is a D-U-N-S® Number considered as non-active?](#)

[When are there no hits?](#)

TSPARMCD = SPONSOR

[Search By Company name](#)[Search By Telephone Number](#)

Company Name*:

Address:

City:

State*:

State

▼

Zip Code:

Country*:

United States of America

▼

Search Now

TSPARMCD = SPONSOR

- ▶ Pro's and Con's of the UPIK® portal vs. d&b number look-up
 - searches on the UPIK® portal appeared to be error prone
 - searches for the same term, minutes apart, lead to successful and unsuccessful results
 - method of operation remains unclear
 - provides full DUNS number
- d&b number look-up generates faster results to check if a company is registered with a DUNS number
- not as error prone as the UPIK® portal
- need to have an account to receive requested DUNS number via e-mail

TSPARMCD = SPONSOR

- ▶ Personal recommendations for a successful search:
 - Use UPIK® portal
 - Search for the full, official company name and the country (and state) of the corresponding headquarter
 - If this result is not successful, make sure that the company is indeed registered with d&b via the d&b number look-up function
 - Search for parts of the full company name
 - Keep in mind the city of the corresponding headquarter and the official form of organization of the company
 - Include the company name into TSVAL and the DUNS number into TSVALCD

TSPARMCD = INDIC

- ▶ Informs about the trial indication
- ▶ “The condition, disease or disorder that the clinical trial is intended to investigate or address.” (SDTM Terminology 2019-06-28)
- ▶ Usually found in the clinical study protocol
- ▶ Needs to be coded according to SNOMED CT
- ▶ Include SNOMED CT term into TSVAL and the corresponding code into TSVALCD
- ▶ SNOMED CT term needs to be approved by the sponsor

TSPARMCD = INDIC

SNOMED CT Browser

Release: International Edition 2019-07-31

Perspective: Full

Feedback

About

SNOMED International

Taxonomy

Search

Favorites

Refset

Search

Options

Search Mode: Partial matching search mode

Status: Active concepts only

Group by concept

Filter results by Language

english 15

Filter results by Semantic Tag

disorder 5

observable entity 1

procedure 1

finding 1

situation 1

Type at least 3 characters Example: shou fra

Angina pectoris

15 matches found in 0.281 seconds.

Angina pectoris	Angina (disorder)
H/O: angina pectoris	History of angina pectoris (situation)
AP - Angina pectoris	Angina (disorder)
Variant angina pectoris	Prinzmetal angina (disorder)
History of angina pectoris	History of angina pectoris (situation)
Angina pectoris with documented spasm	Coronary artery spasm (disorder)
History of angina pectoris (situation)	History of angina pectoris (situation)
Treadmill stress test negative for angina pectoris	Treadmill stress test negative for angina pectoris (finding)
Treadmill stress test negative for angina pectoris (finding)	Treadmill stress test negative for angina pectoris (finding)

Concept Details

Expression Constraint Queries

Concept Details

Summary

Details

Diagram

Expression

Refsets

Members

References

Stated

Inferred

Parents

- Chest pain (finding)
- Disorder characterized by pain (disorder)
- Ischemic heart disease (disorder)
- Pain of cardiovascular structure (finding)

Angina (disorder) ☆

SCTID: 194828000

194828000 | Angina (disorder) |

- en Angina
- en Stenocardia
- en Anginal syndrome
- en Angina pectoris
- en Ischemic heart disease - angina
- en AP - Angina pectoris
- en Cardiac angina
- en Angina (disorder)
- en Ischaemic heart disease - angina

Finding site → Heart structure
Associated morphology →
Structural change due to ischemia

TSPARMCD = TDIGRP

- ▶ Describes the diagnosis group(s) of a clinical trial, coded according to SNOMED CT
- ▶ “A grouping of individuals on the basis of a shared procedure or disease, or lack thereof.” (SDTM Terminology 2019-06-28)
- ▶ Parameter doesn't need to be included into TS if study population is comprised of only healthy subjects
- ▶ Information about the diagnosis group(s) can be obtained from the clinical study protocol

TSPARMCD = TDIGRP

- ▶ Diagnosis group can:
 - align with trial indication
 - be a more specific manifestation of an umbrella term represented by the „INDIC“ parameter
 - can stand in relation to the trial indication
- ▶ Include SNOMED CT term into TSVAL and the corresponding code into TSVALCD
- ▶ SNOMED CT values should be approved by the sponsor

TSPARMCD = TRT

- ▶ Represents the investigational therapy or treatment based on the naming convention of FDA's Global Substance Registration System (GSRS): the Unique Ingredient Identifier (UNII)
- ▶ UNII terms/codes identify ***active ingredients*** of the trial medication
- ▶ Parameter "TRT" needs to be included in the TS domain if the study type is an interventional one

TSPARMCD = TRT

**U.S. Food and Drug Administration**
Protecting and Promoting Your Health

U.S. National Library of Medicine

Substance Registration System - Unique Ingredient Identifier (UNII)

Search

Substance Registration System

Information available for 106,208 substances.

(automatic) ▼

(automatic) ▼

Search

- ▶ [Show examples \(including wildcard searches using *\)](#)
- ▶ [UNII List download \(updated Jul 12, 2019\)](#)
- ▶ [About Substance Registration System](#)

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U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894
National Institutes of Health, Health & Human Services
Freedom of Information Act
Last updated: Oct 2019



TSPARMCD = TRT

- ▶ Searching for the correct UNII term/code can become a complicated matter for the TS domain creator
- ▶ Knowledge about the nature/complexion of the trial medication needed
- ▶ Input from the appropriate persons within sponsor's organisation can be needed, respectively any search result should be communicated and approved by the sponsor

TSPARMCD = TRT

► Personal approach/recommendation:

- Gather available information about the ingredients of the trial medication (e.g. from the clinical study protocol)
- Check the GSRS for (an) available UNII code(s) for the ingredient(s)
- Correspond findings or lack thereof to the sponsor
- If sponsor agrees with gathered UNII codes, include name(s) of ingredient(s) in TSVAL and UNII code in TSVALCD; if sponsor does not agree, sponsor should provide correct UNII term(s) and code(s), if available

TSPARMCD = TRT

► Personal approach/recommendation:

- If no entry in GSRS is available for ingredient(s) of trial medication, sponsor needs to decide on further proceeding:
- The FDA recommends that sponsors obtain UNII codes for yet unapproved substances “as early in drug development as possible” (Study Data Technical Conformance Guide, page 39)
- Other possibilities: do not fill TSVAL and TSVALCD for this entry but fill TSVALNF with a Null Flavor enumeration and TSVCDREF with “ISO 21090”; alternatively use the substance name of the trial medication for TSVAL, do not fill TSVALCD, therefore stating only the trial medication, respectively the active ingredient of the trial medication, without any registered code

TSPARMCD = PCLAS

- ▶ Holds information about the established pharmacological class of the active substance(s) of the trial medication
- ▶ *What is a pharmacological class?*

TSPARMCD = PCLAS

- ▶ FDA definition of a pharmacological class:
 - “Pharmacologic class is a group of active moieties (drugs) that share scientifically documented properties and is defined on the basis of any combination of three attributes of the active moiety:
 - Mechanism of Action (MOA) - Pharmacologic action at the receptor, membrane, or tissue level
 - Physiologic Effect (PE) - Pharmacologic effect at the organ, system, or whole body level
 - Chemical Structure (CS)”*
- ▶ (* <https://www.fda.gov/industry/structured-product-labeling-resources/pharmacologic-class>)

TSPARMCD = PCLAS

- ▶ FDA definition of an established pharmacological class:
 - “An FDA “Established Pharmacologic Class” (EPC) text phrase is a pharmacologic class associated with an approved indication of an active moiety (drug) that the FDA has determined to be scientifically valid and clinically meaningful.” *
- ▶ scientifically valid: PC is known, relevant and specific to the indication
- ▶ clinically meaningful: helps professionals to understand physiological effects related to the indication and undesirable effects associated with the drug/PC
- ▶ (* <https://www.fda.gov/industry/structured-product-labeling-resources/pharmacologic-class>)

TSPARMCD = PCLAS

- ▶ EPC is based on MED-RT and used in the “Indication and Usage” section of the “Highlights of prescribing information”

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING

See full prescribing information for complete boxed warning.

- Text (4)
- Text (5.x)

RECENT MAJOR CHANGES

Section Title, Subsection Title (x.x) M/YYYY
Section Title, Subsection Title (x.x) M/YYYY

INDICATIONS AND USAGE

PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)

Limitations of Use

Text (1)

DOSAGE AND ADMINISTRATION

- Text (2.x)
- Text (2.x)

DOSAGE FORMS AND STRENGTHS

Dosage form(s): strength(s) (3)

CONTRAINDICATIONS

- Text (4)
- Text (4)

WARNINGS AND PRECAUTIONS

- Text (5.x)
- Text (5.x)

ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Text (7.x)
- Text (7.x)

USE IN SPECIFIC POPULATIONS

- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

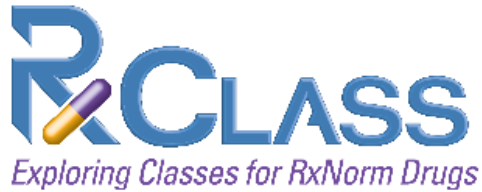
Revised: M/YYYY

TSPARMCD = PCLAS

- ▶ Personal suggestion for finding the correct established pharmacological class of a trial medication:
 - Use the TSVAL value for parameter “TRT” (preferably a UNII term) to search for the established pharmacological class of a substance, using the RxClass browser of the U.S. National Library of Medicine
 - Use the search function “by RxNorm drug name/id”

A screenshot of the RxClass web application interface. It features a dark blue header bar. On the left, there are three radio buttons for search criteria: "by class name/id", "by RxNorm drug name/id" (which is selected), and "show source data". To the right of these is a link that says "Edit Drug Sources". On the far right of the header is a search bar with the text "Gabapentin" entered. A magnifying glass icon is to the right of the search bar, and a small "x" icon is inside the search bar on the left side.

TSPARMCD = PCLAS



Gabapentin

☐ by class name/id ☒ by RxNorm drug name/id ☐ show source data [Edit Drug Sources](#)

20 classes found for drug '**Gabapentin**'

[Ingredient(s):gabapentin]

[Anti-epileptic Agent in EPC \(has_EPC\)](#)

class: **Anti-epileptic Agent** / id: **N0000175753** / class type: **EPC** / [show context](#)

TSPARMCD = PCLAS

- ▶ Any search result for the EPC needs to be approved by the sponsor
- ▶ If no pharmacological class is available for the trial medication the FDA recommends:
 - “If the established pharmacologic class is not available for an active moiety, then the sponsor should discuss the appropriate MOA, PE, and CS terms with the review division. For unapproved investigational active moieties where the pharmacologic class is unknown, the PCLAS record may not be available.”
(Study Data Technical Conformance Guide v4.3, PDF page 41)
- ▶ ➔ Nullflavor value in TSVALNF
- ▶ ➔ Alternative (?): Anatomical Therapeutic Chemical (ATC) code

- ▶ Filling some of the TS parameter requires knowledge that goes beyond the area of Statistical Programming or Data Management
- ▶ TS creating CRO persons should always make sure to get approval by their contact persons on the sponsor's side
- ▶ Contact person on sponsor's side should locate appropriate persons within their organisation for approval, respectively provision of needed TS information



Thank You!

Questions?