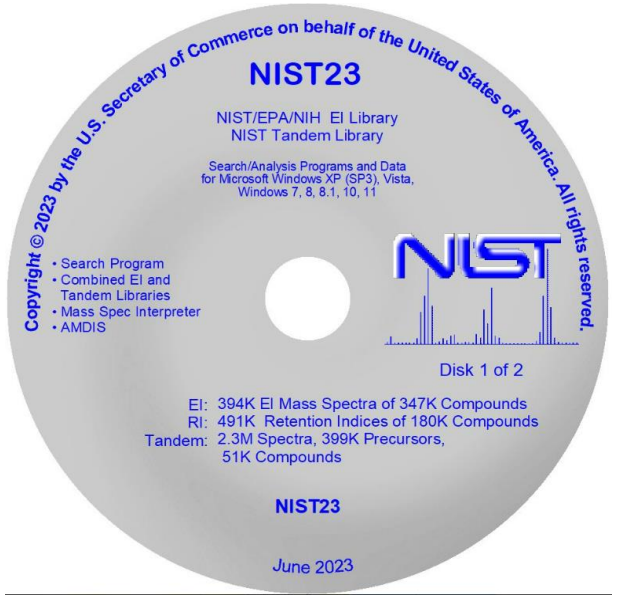
Part 0: Changes in Tandem (MS/MS) NIST23 Search Program (V3.0)

James Little
Mass Spectral Interpretation Services
4/28/2023

EI, RI

Full: EI, Tandem, RI



Tandem (MS/MS)

RI Only

*Didn't want to renumber the original courses, so named first one "0", no zero in Roman numerals, only "nullus" to indicate nothing

List of Changes in NIST23 Search from User Manual

What's New in MS Search Program v.3.0

The following features were added to the current version 3.0 (2023), distributed with NIST 23, as compared to ver. 2.4, distributed with NIST 20.

- Major Spectrum Type choice (EI, Tandem, Peptide, All) helps to suppress display of search parameters most probably not used.
- Name search has been improved by increasing search field from 16 to 249 characters; the list of names has been split into two windows: compound list in the upper window and spectra list in the lower window.
- The list of **Other Databases** (non-mass spectra) has been significantly extended.
- *NEW.* A Partial Spectrum Search method has been added.
- AI estimated RI are displayed in EI Hit List and is used for EI search with RI match factor correction instead of missing semi-standard non-polar RI in a Hit.
- Hovering a mouse pointer around a peak in a spectrum plot displays peak annotation.

Changes

- Term "In-source/EI with accurate ion *m/z*" replaced with "HiRes No Precursor".
- "Penalize rare compounds" EI library search option has been retired.
- Clicking on the InChIKey in the Text Information window takes you to an Internet Google Search rather than to PubChem.

Note: Manual has hyperlinks in "***blue***"

NIST and AMDIS Manuals Link

Large Increase in Tandem Spectra NIST23

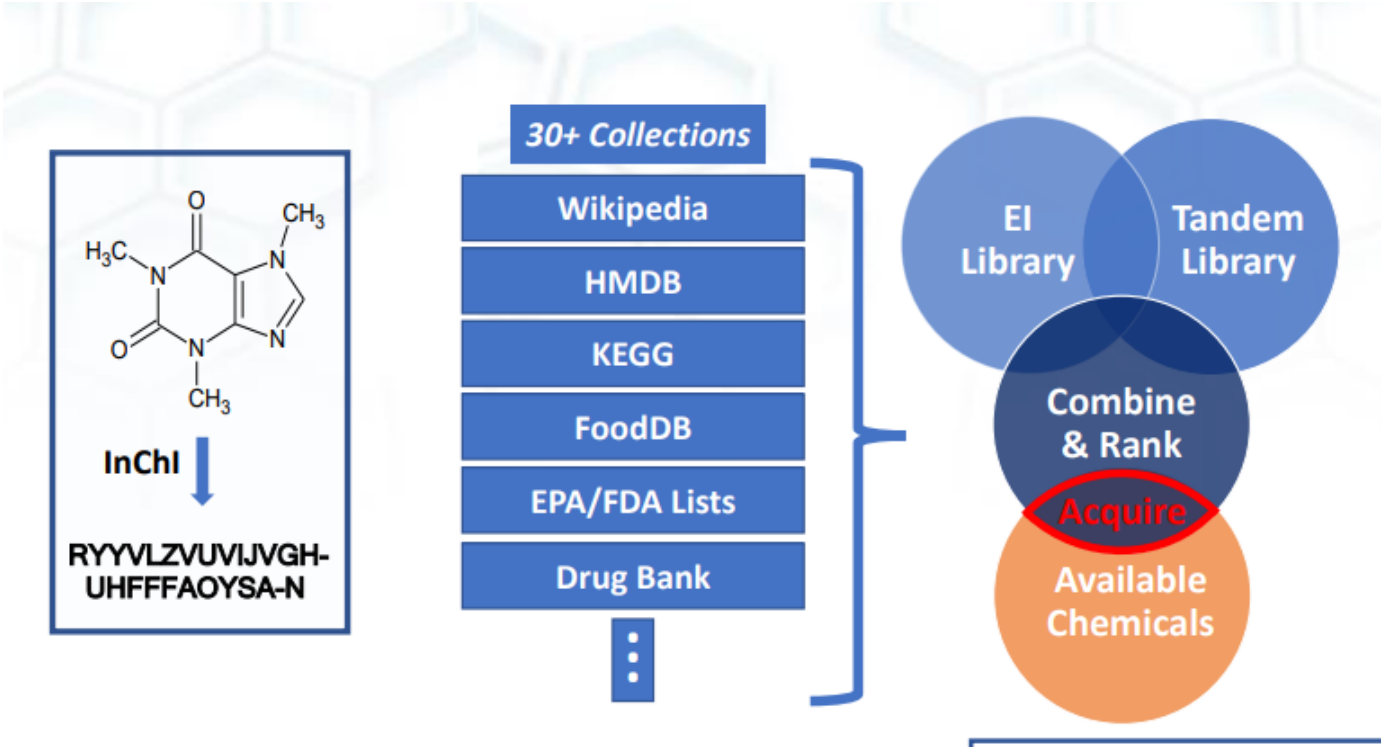
NIST Tandem Mass Spectral Library
2023 Release

51,501 Compounds, 60% More than 2020
400 K Precursor Ions – 2.4 M Spectra

Fragmentation Methods	Precursor Ion Types
49,590 HRAM (High Res Accurate Mass) Compounds	44,191 Protonated
50,071 QTOF, HCD, IT-HRAM, QqQ Compounds	19,620 Deprotonated
49,561 Ion Trap Compounds (Low Res., up to MS^4)	14,318 Water/Ammonia Loss
561 APCI HRAM Compounds	44,547 Other In-Source Generated

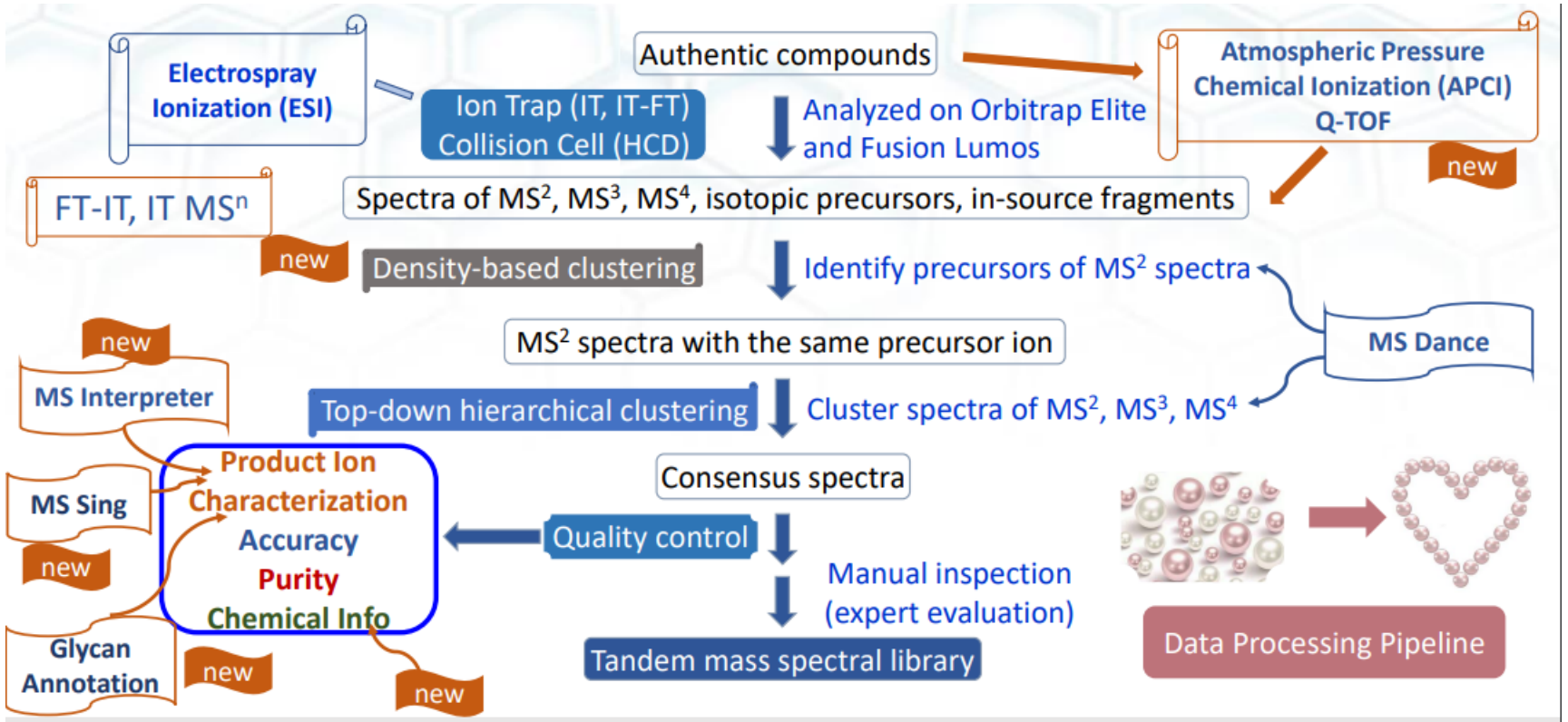
NIST Promotional Information and Statistics on Tandem Library

New Compound Selection Process



[NIST Promotional Information and Statistics on Tandem Library]

Procedure of Extending the NIST Tandem Mass Spectral Library



X. Yang, P. Neta, S. Stein. Extending A Tandem Mass Spectral Library to Include MS² Spectra of Fragment Ions Produced In-Source and MSⁿ Spectra. *J. Am. Soc. Mass Spectrom.* November 2017, 28: 2280–2287.

X. Yang, P. Neta, S. Stein. Quality Control for Building Libraries from Electrospray Ionization Tandem Mass Spectra. *Anal. Chem.*, 2014, 86: 6393-6400.

[ASMS Presentation on Details of Release]

Watch the Current Webinar for V3.0 Changes and Then View Additional Videos on My Website to Complete Training

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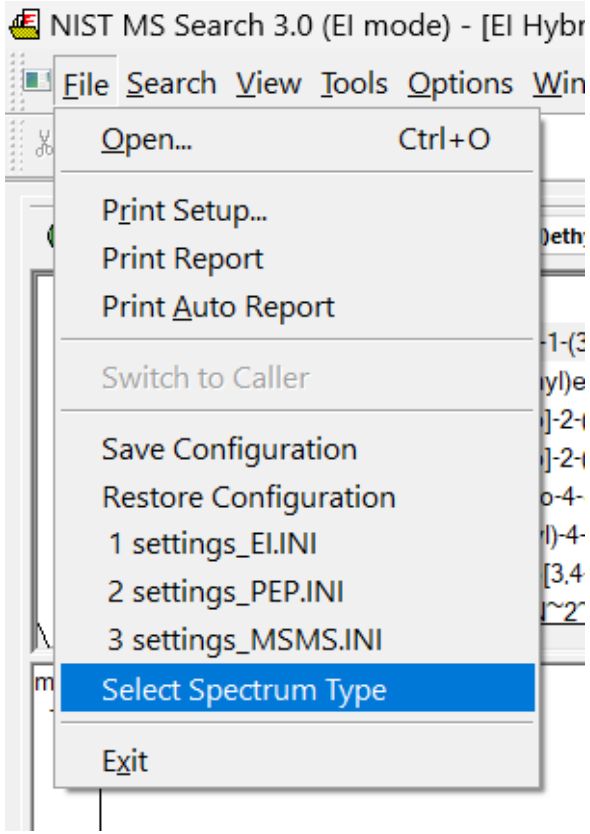
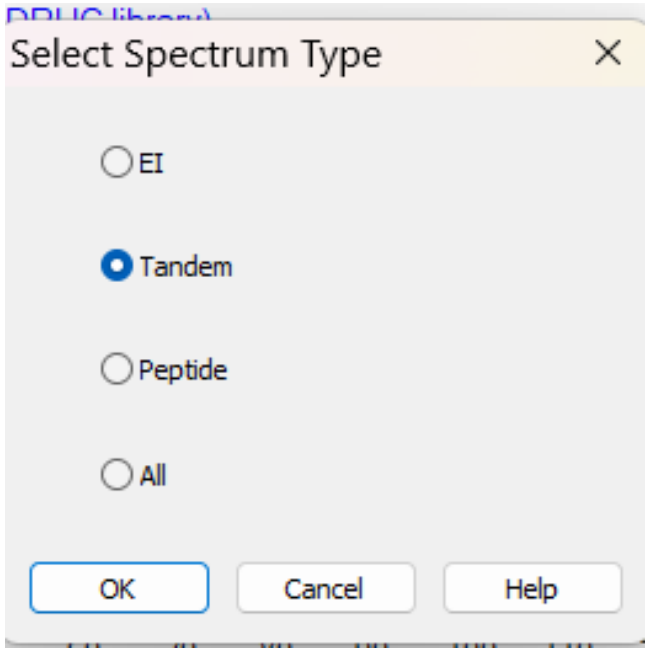
Link to MSMS NIST Search Course

Simplified Menus Separating Tandem and EI Search Options

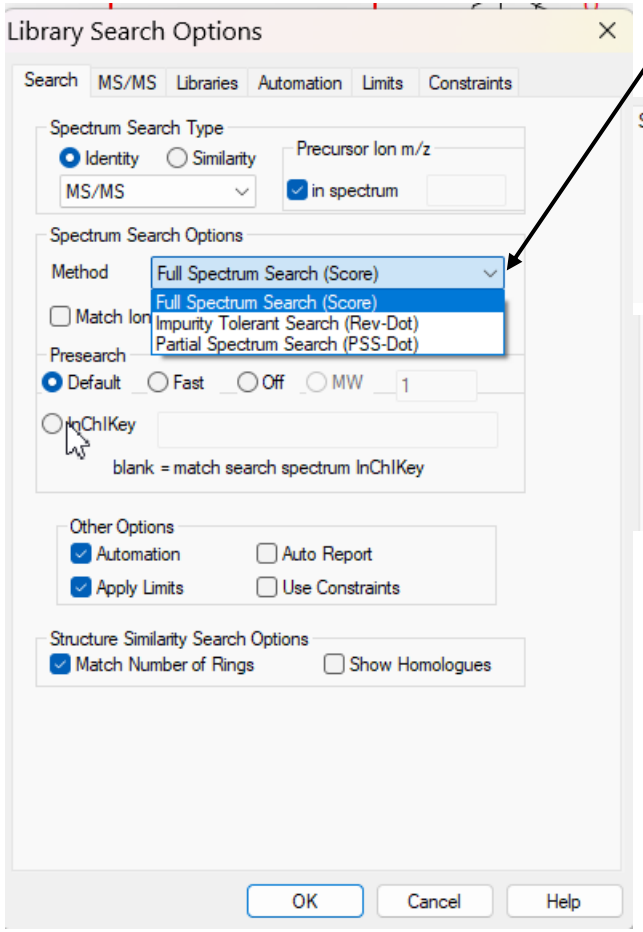
Only **Present Version 3.0**



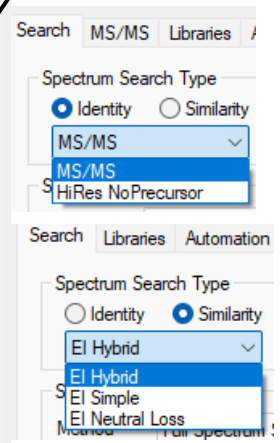


Simplified EI Library Search Options Menu: Only Tandem (MS/MS) Options!

Version 3.0

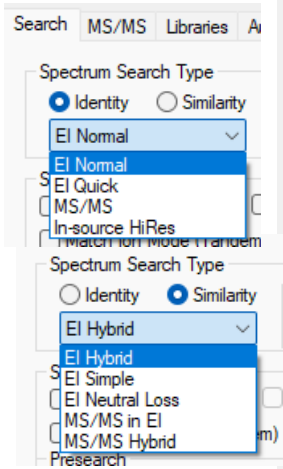


2



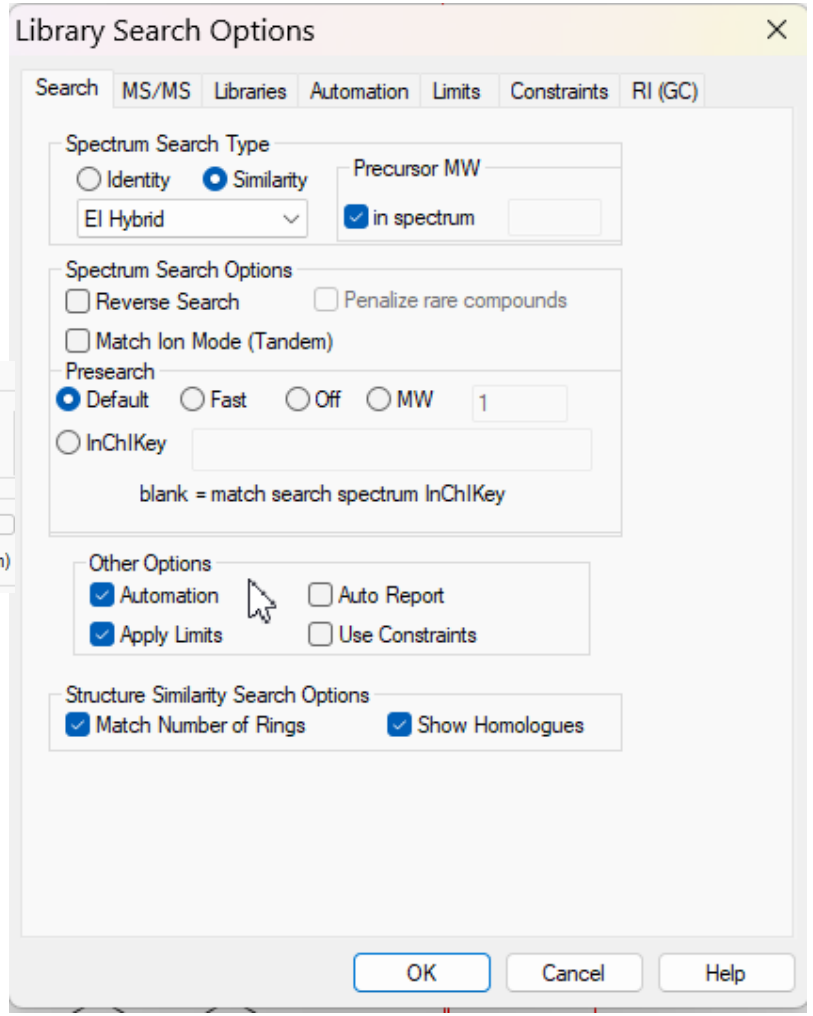
1

1



1. Only the Tandem search options shown in Identity and Similarity searches for V3.0
2. Pull down menu for searches, New Partial Spectrum Search

Version 2.4



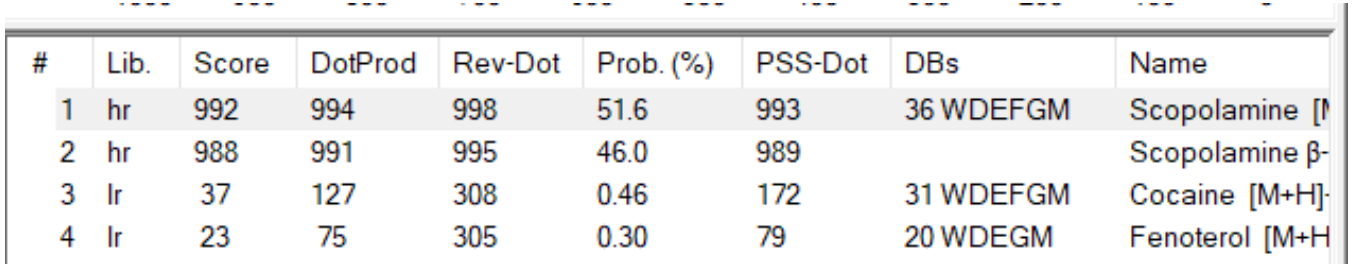
New InChIKey Google Link to Internet in V3.0 Replaces PubChem Link in V2.4

- Much improved link to Google search when clicking on InChIKey
- Often useful to select image tab in Google results to see only images
- PubChem should still shown in the search results, but only indirectly

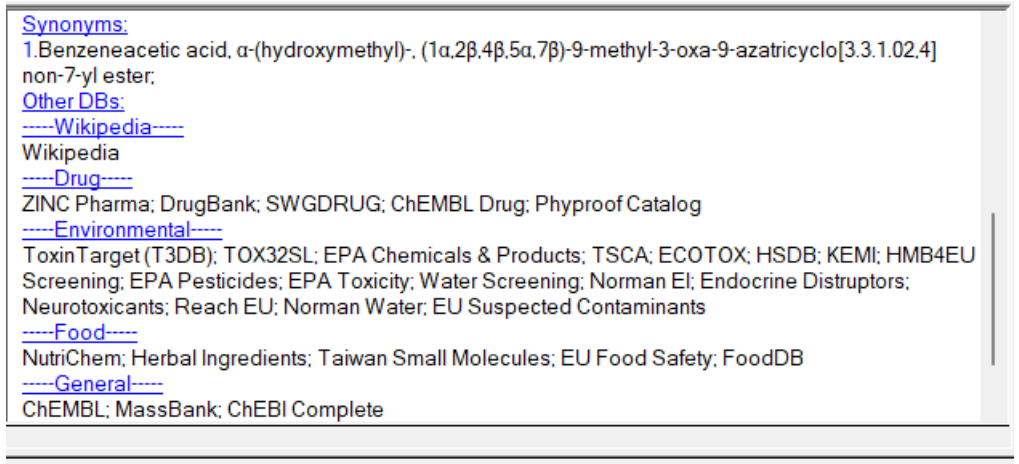
Comment: NIST Mass Spectrometry Data Center
Related CAS#: 51343
Notes: Spec=Consensus Nreps=19/19 Mz_diff=-4.6ppm micromol/L in water/acetonitrile/formic acid (50/50/0.1) Vial_ID=830 Metabolite_2015_ID=49904
Ion mode: P
Instrument: Thermo Finnigan Elite Orbitrap
Ionization: ESI
Collision gas: N2
Sample inlet: direct flow injection
Spectrum type: MS2
InChIKey: STECJAGHUSJQJN-PMFPHFEJSA-N Non-stereo
Synonyms:
1.Benzeneacetic acid, α-(hydroxymethyl)-, (1α,2β,4β,5α,7β)-9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4] non-7-yl ester;

Databases Reference in Search Results Significantly Extended

- Many more databases referenced
- Results display shows abbreviations and the total number of references
- Search results show full name of the database
- List of databases in NIST PDF document shown on next slide
- If similar hit results for compounds with different structures, should consider the one with highest number of database references in absence of sample history



#	Lib.	Score	DotProd	Rev-Dot	Prob. (%)	PSS-Dot	DBs	Name
1	hr	992	994	998	51.6	993	36 WDEFGM	Scopolamine [M
2	hr	988	991	995	46.0	989		Scopolamine β-
3	lr	37	127	308	0.46	172	31 WDEFGM	Cocaine [M+H]-
4	lr	23	75	305	0.30	79	20 WDEGM	Fenoterol [M+H



Synonyms:
1.Benzeneacetic acid, α-(hydroxymethyl)-, (1α,2β,4β,5α,7β)-9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4]non-7-yl ester;
Other DBs:
-----Wikipedia-----
Wikipedia
-----Drug-----
ZINC Pharma; DrugBank; SWGDRUG; ChEMBL Drug; Phyproof Catalog
-----Environmental-----
ToxinTarget (T3DB); TOX32SL; EPA Chemicals & Products; TSCA; ECOTOX; HSDB; KEMI; HMB4EU Screening; EPA Pesticides; EPA Toxicity; Water Screening; Norman EI; Endocrine Distruptors; Neurotoxicants; Reach EU; Norman Water; EU Suspected Contaminants
-----Food-----
NutriChem; Herbal Ingredients; Taiwan Small Molecules; EU Food Safety; FoodDB
-----General-----
ChEMBL; MassBank; ChEBI Complete

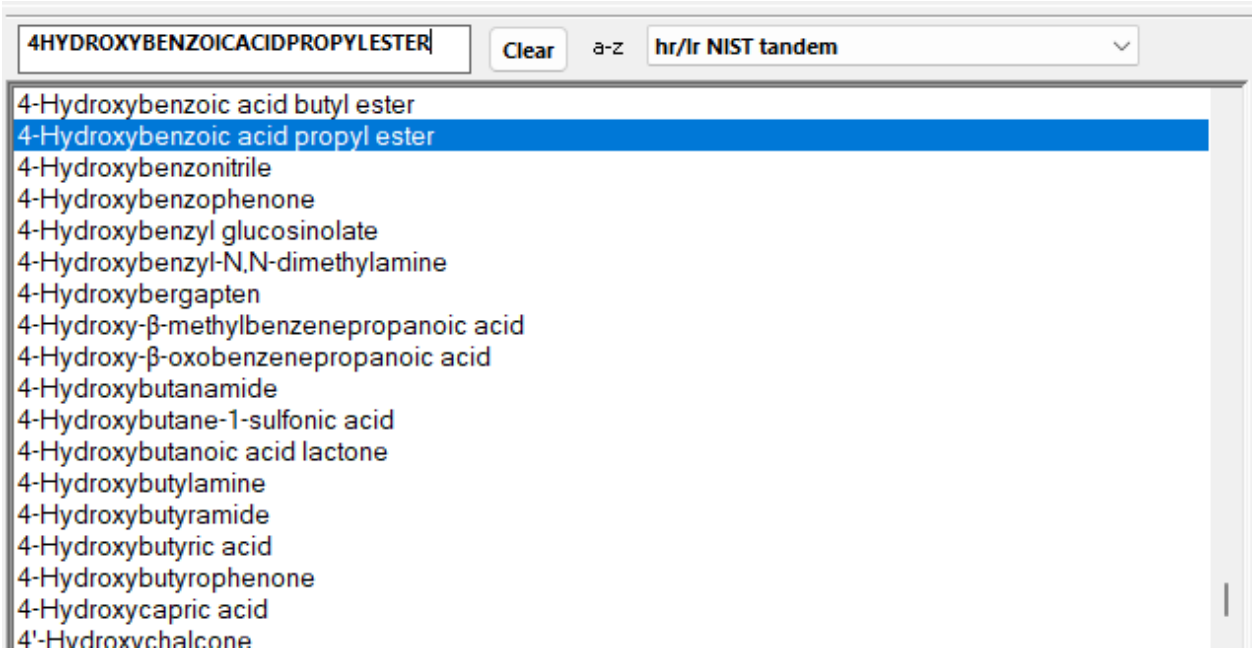
List of Databases in Search Results in NIST PDF File

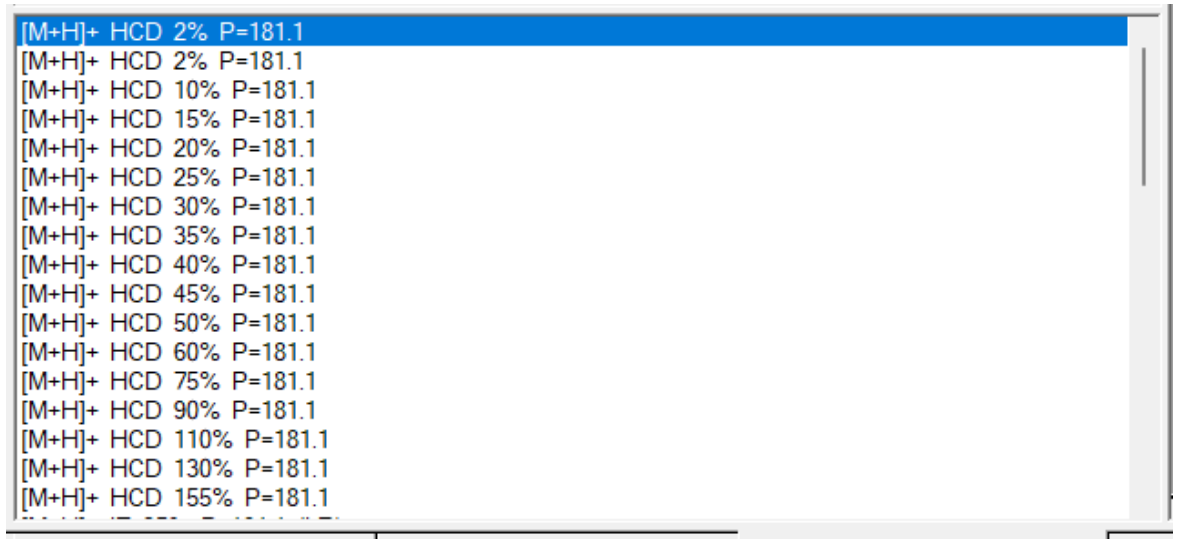
Catalog Name	Generic Title	Class	Subclass	Description	URL
EPACOMPTOX_EPA official InertIngredients_Nov2019	EPA Pesticide Inert	(C) Contaminants	Pesticide	Inert pesticide ingredients, Food and Nonfood use, as defined by EPA are those inert ingredients approved for use in pesticide products applied to food that have either tolerances or tolerance exemptions in the Code of Federal Regulations (CFR), 40 CFR part 180, or where no residues are found in food	https://comptox.epa.gov/dashboard/chemical-lists/PESTINERTS
EPACOMPTOX_Pesticides InertFinder_Nov2020	EPA Pesticide Inert2	(C) Contaminants	Pesticide	InertFinder is an online database for searching substances used as inert ingredients in pesticide products	https://comptox.epa.gov/dashboard/chemical-lists/INERTNONFOOD
EPACOMPTOX_PLASTICS NORMAN 2019	Plastic Contaminants	(C) Contaminants	Extractible & Leachable	Database of Chemicals possibly (List B) associated with Plastic Packaging (CPPdb)	https://comptox.epa.gov/dashboard/chemical-lists/CPPDBLISTB
Thermo_AdditivesList2022	Thermo Additives	(C) Contaminants			
EPACOMPTOX_ZINC15 pharmaceuticals	ZINC Pharma	(D) Drug		Pharmaceuticals retrieved from ZINC15, curated and provided by Reza Aalizadeh, University of Athens	https://comptox.epa.gov/dashboard/chemical-lists/ZINC15PHARMA
TMIC_DrugBankFY22	DrugBank	(D) Drug		DrugBank database (TMIC/Univ. Alberta)	https://go.drugbank.com/
EPACOMPTOX_SWGDRUG_NOv2019	SWGDRUG	(D) Drug	Forensics	The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) has compiled a mass spectral library from a variety of sources, containing drugs and drug-related compounds	https://comptox.epa.gov/dashboard/chemical-lists/SWGDRUG
ChEMBL2021_drugs	ChEMBL Drug	(D) Drug		Compounds labeled as drugs in CHEMBL	https://www.ebi.ac.uk/chembl/g/#browse/drugs
Phyproof_Reference Substance Catalogue2022-2023_vFeb_2022	Phyproof Catalog	(D) Drug			https://phyproof.phytolab.com/en/service/x/download/
TMIC_T3db	ToxinTarget (T3DB)	(E) Environmental	Pesticide	Toxin and Toxin Target Database (T3DB)	http://www.t3db.ca/
EPACOMPTOX_TOX21SL_Feb2017	TOX32SL	(E) Environmental	Pesticide	TOX21SL is a list of unique DSSTox substances comprising the original screening library for the Tox21 program, a multi-federal agency collaborative among US EPA, the NIH National Toxicology Program (NTP) and NCATS, and the FDA	https://comptox.epa.gov/dashboard/chemical-lists/TOX21SL
EPACOMPTOX_CPDATFY22	EPA Chemicals & Products	(E) Environmental	Contaminants	list of chemicals reported in the EPA's Chemical and Products Database	https://comptox.epa.gov/dashboard/chemical-lists/CPDAT
TSCA_wStructuresFinal	TSCA	(E) Environmental	Commercial	Toxic Substances Control Act (old list)	
ECOTOX_EPAcomptox	ECOTOX	(E) Environmental	Toxicity	The ECOTOX Knowledgebase is a comprehensive, dynamic, curated database that summarizes chemical environmental toxicity data on aquatic life, terrestrial plants, and wildlife	https://comptox.epa.gov/dashboard/chemical-lists/ECOTOX_v2
EPACOMPTOX_Hazard Substances Databank_Nov2019	HSDB	(E) Environmental	Toxicity	HSDB is a toxicology database that focuses on the toxicology of potentially hazardous chemicals	https://comptox.epa.gov/dashboard/chemical-lists/HSDB2019
EPACOMPTOX_PFASMASTER Sep2020	PFAS List	(E) Environmental	Contaminants	PFAS Master List of PFAS Substances	https://comptox.epa.gov/dashboard/chemical-lists/PFASMASTER
EPACOMPTOX_KEMIMARKETFY22	KEMI	(E) Environmental	Commercial	KEMI Market List contains chemicals expected to be on the market, with a focus on the EU market	https://comptox.epa.gov/dashboard/chemical-lists/KEMIMARKET
EPACOMPTOX_CECSCREENFY22	HMB4EU Screening	(E) Environmental	Contaminants	HBM4EU CECscreen is a suspect screening list for Chemicals of Emerging Concern (CECs) plus metadata and predicted Phase 1 metabolites	https://comptox.epa.gov/dashboard/chemical-lists/CECSCREEN
EPACOMPTOX_OPPIN_Oct2019	EPA Pesticides	(E) Environmental	Pesticide	CATEGORY|EPA|PESTICIDES: Office of Pesticide Programs Information Network	https://comptox.epa.gov/dashboard/chemical-lists/OPPIN
EPACOMPTOX_TOXVALFY22	EPA Toxicity	(E) Environmental	Toxicity	The Toxicity Values database is delivered via the Hazard Tab in the CompTox	https://comptox.epa.gov/dashboard/chemical-lists/TOXVAL_V5

Link to List of Databases

Very Much Improved Name Search in V3.0 NIST Search

- Number of characters searched increased from 16-249
- Greatly improves results for specific compound of interest
- When typing in request, spaces, commas, etc. are ignored
- Can toggle to ignore numbers if desired with a-z button, but should include when specific isomer desired
- Results at bottom of screen show tandem spectra obtained at different conditions
- Only one library searched at a time





In Summary

- Use Part O to understand changes from V3.0 to 2.4
- Then view Parts I-VIII to gain complete understanding of the software for unknown identification
- In general, all major functions and concepts are the same
- NIST just simplified the Library Search options menu
- Created an EI specific one and a Tandem (MS/MS) specific one
- Many other nice features added including improved name search, Google/InChIKey search, etc.
- See total list in manual pg 23 for other minor changes

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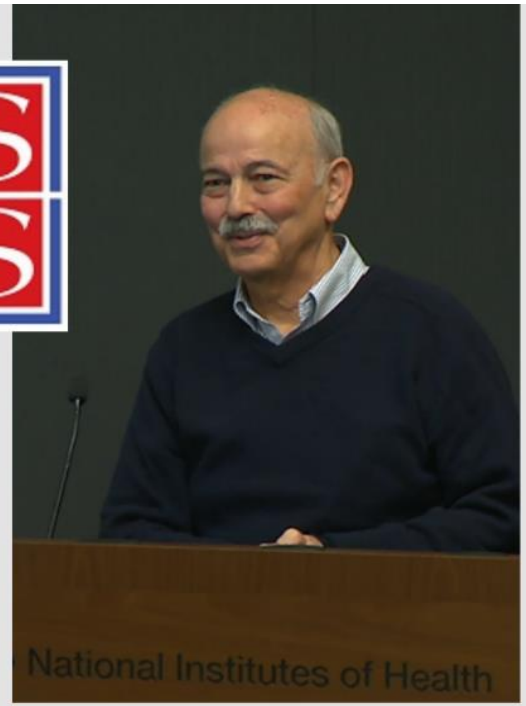
Link to MSMS NIST Search Course

Webinar Dedicated to Sandy for All His Critical Input on NIST23…



Sanford (Sandy) P. Markey

1942 - 2022

A member of ASMS since 1968

ASMS Board member 1992-1993

A lifetime career at NIH (NIMH and NIST)

… Sandy will be missed