Zoom Cloud Meetings | Zoom Meeting | 2022-04-05 16:06:28 UTC | norwid

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View

nbehrnd | Jonathan Goodman | Jonathan Goo... | Thomas Doern...

nbehrnd | Jonathan Goodman | Jonathan Goodman | Thomas Doerner

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burt.leland (OpenEye) | Ingvar Lagerstedt | Marc Nicklaus | Ulrich Schatzschr

1/3

Bob Belford | Falko FRENZE... | Andrey Yerin -... | Aleksandr Beli...

Bob Belford | Falko FRENZEL (BfR, G... | Andrey Yerin - ACD/Lab... | Aleksandr Belinskiy

Alexander Awad | Daniel Lowe | Evan Bolton | Richard Kidd

Alexander Awad | Daniel Lowe | Evan Bolton | Richard Kidd

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Chat

Gudrun Gygli to Everyone 06:03 PM

Sorry, have to leave for another meeting. Thanks for all the intersting info!

Sunghwan Kim, NIH to Everyone 06:04 PM

Does the current version of Polymer-InChI distinguish (1) between LDPE and BDPE (that is, different polymers from the same monomer) and (2) polymers with different degree of polymerization (i.e., polymers with different numbers of monomers).

Sorry, LDPE vs HDPE (low- vs high-density PEs)

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Heather
Heather

Lars B
Lars B


ggrethe

Peter Linstrom
Peter Linstrom


Blanke


Steve Heller

Leah McEwen
Leah McEwen


Hinnerk Rey - Else

2/3


Nau, Heike (ELS-FRK)

Schwörer, Mar...
Schwörer, Markus (ELS...

Sunghwan Ki...
Sunghwan Kim, NIH

Nicki Davis
Nicki Davis (She/Her)

2/3

Roger Sayle
Roger Sayle

Ian B
Ian B


Alex Henderson, Manc...


Sonja Herres-Pawlis

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Sunghwan Ki...
Sunghwan Kim, NIH

Nicki Davis
Nicki Davis (She/Her)

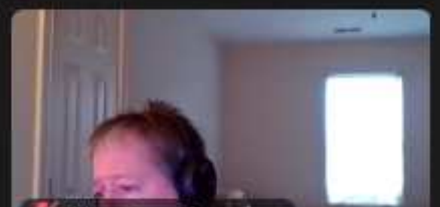
Roger Sayle
Roger Sayle

Ian B
Ian B


Henderson, Manc...


Sonja Herres-Pawlis

Anders
Anders


Hunter Moseley

3/3


rudy potenzone

Mick Kappler
Mick Kappler


Chris Jakober (CARB)

Yulia Borodina
Yulia Borodina

Barrie Walker
Barrie Walker


Gabe Weatherhead

Sandra Simon
Sandra Simon

Jane
Jane

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Sandra Simon | Jane | Markus Sitzmann

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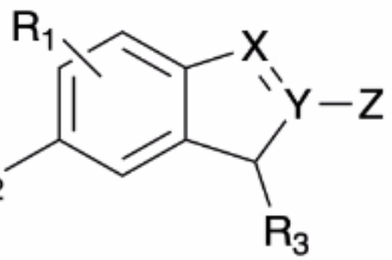
More Complex Variability

Use Te in place of Zz because RDKit can handle it



R_1 = H, Me
R_2 = Me, Et, Pr, Bu
R_3 = Ph, tolyl
X = N, CH
Y = C, N+
Z = Cl, CH_2Cl

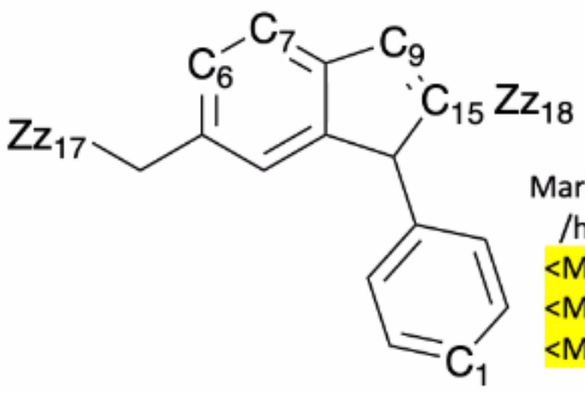
128 distinct structures

Enumerate structures

CANONICAL!
(based on template)

Software available on Github

Generate from molfile v3000



MarkInChI=1B/C16H12Zz2/c17-10-11-6-7-13-9-15(18)16(14(
/h1-9,16H,10H2
<M>H!C!C2H5Zz/c1-2-3/h2H2,1H3!C3H7Zz/c1-2-3-4/h2-3H
<M>CH2ClZz/c2-1-3/h1H2!Cl
<M>9-C!N<M>15-C!N+<M>1H-C!H<M>6H,7H-C!H

Abdullah Kattineh

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nbehrnd

Jonathan Goo...

nbehrnd

Jonathan Goodman

Jonathan Goodman

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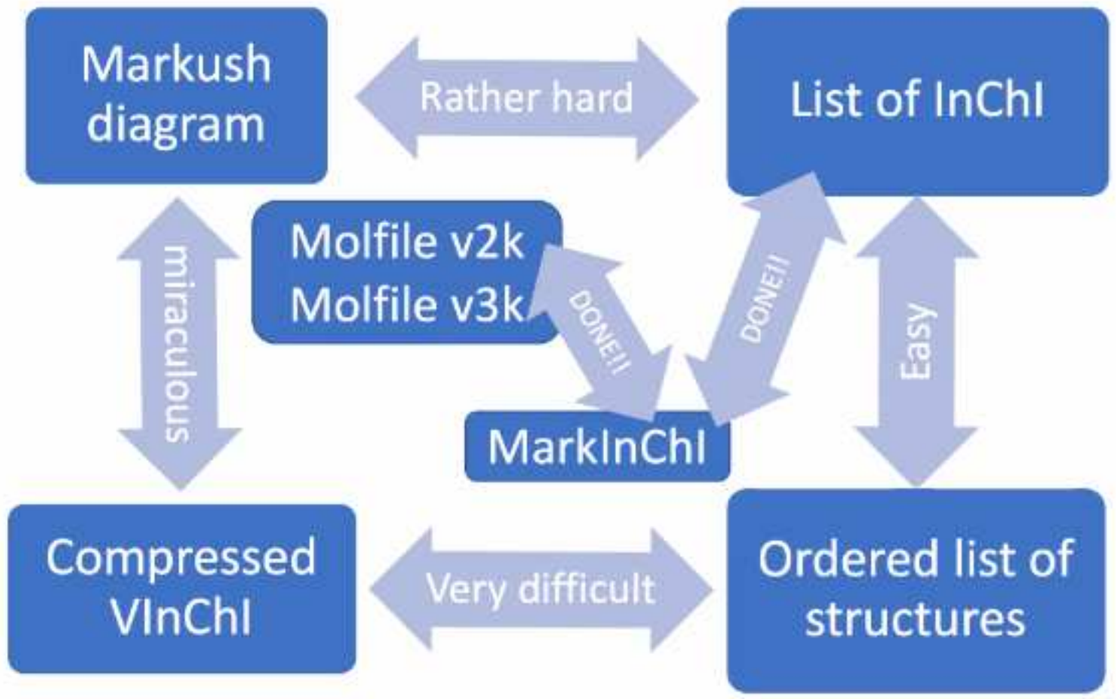
What is to be done?

a) Assume there are millions of structures in each Markush

b) Need to be able to calculate ∩ and ∪



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Tautomerism

Tautomers are isomers that can readily transform into each other through chemical equilibrium reactions

Strongly environment-dependent (pH, solvent, temperature, time, ...)

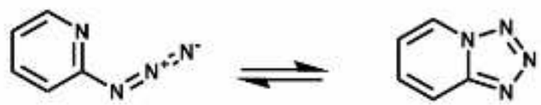
- Prototropic tautomerism:

intramolecular movement of a hydrogen atom

enol form *keto form*

- Valence tautomerism:

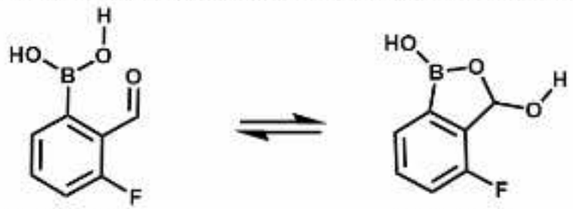
rearrangement of bonds w/o migration of atoms



azide form *tetrazole form*

- Ring-chain tautomerism:

movement of the proton accompanied by opening/closing of a ring



acyclic form *cyclic form*

2

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Chat

Aleksandr Belinskiy to Everyone 07:31 PM

Evan, WIPO is introducing from 07/2022 new standard ST. 26 for representation of biosequences which include in XML scheme description of non-standard aminoacids and chemical modifications, is not clear how the latter information would be used in search. Could your work influence next WIPO standard development for biosequence representation?

Yulia Borodina to Everyone 07:33 PM

SPL standard had introduced it in 2018... A lot of FDA data on proteins are available in this format on DailyMed. InChI is a part of the standard.

Ulrich Schatzschneider to Everyone 07:34 PM

If you want a real challenge: SARS-CoV-2 RNA genome is approx. 30.000 bp = around 1.200.000 atoms ☺

Yulia Borodina to Everyone 07:35 PM

@Ulrich

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burt.leland (OpenEye) | Ingvar Lagerstedt | Marc Nicklaus

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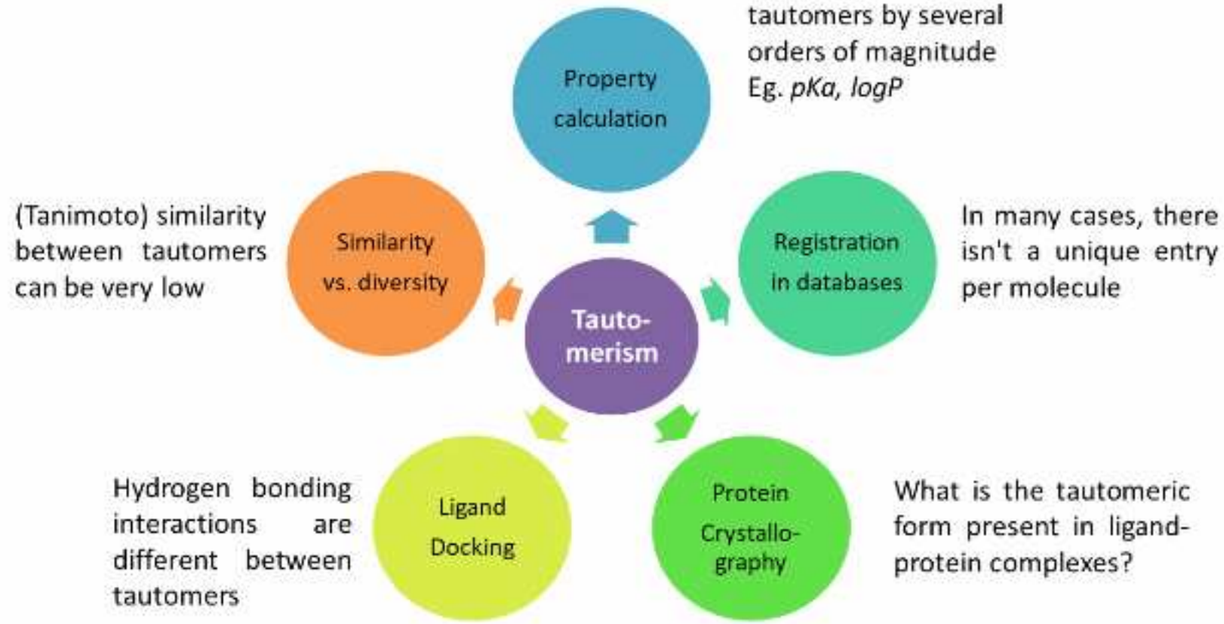
Why worry about tautomers?



The existence of multiple tautomeric forms of the same molecule can create **problems**!!!

3

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burt.leland (OpenEye)

Ingvar Lagers...

Ingvar Lagerstedt

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Not Just an Academic Question

Tautomeric pairs (conflicts) – via NCI/CADD identifiers[1]

[1] Sitzmann *et al.* SAR QSAR Environ. Res. **2008**, *19*, 1–9

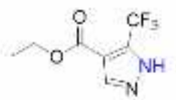
Aldrich Market Select (AMS) database :
5,755,574 molecules (2012-09 version)

31,155 conflicts ⟶ **62,869 molecules**

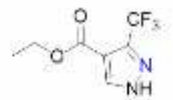
n-tuples	Conflicts
2	30,619
3	514
4	21
5	1

Guasch, L. *et al.* JCIM 56, **2016**, 2149–2161.

Examples (prices per 1 g):



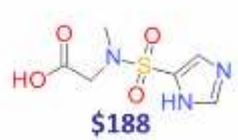
$31



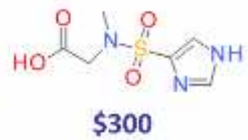
$251

$313

$350



$188



$300

Same original supplier!

4

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burt.leland (OpenEye) | Ingvar Lagerstedt

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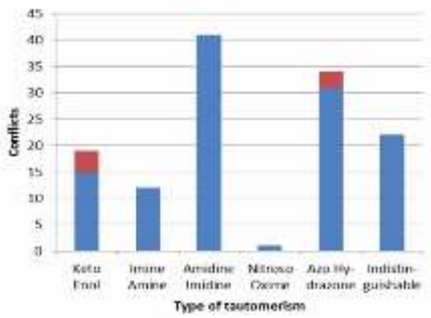
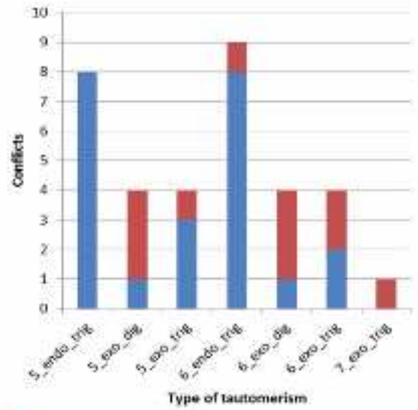
Experimental Verification

Analysis with both ^{1}H NMR and ^{13}C NMR experiments

Prototropic tautomerism



Ring-chain tautomerism



Blue: samples are the same substance. Red: samples are different substances.

Guasch, L. *et al.* JCIM *56*, **2016**, 2149–2161.

5

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Tautomerism is Widespread

Tautomerism is not just interesting, important, and potentially costly – it is widespread:

- Tautomerism possible for an average of 71% structures tautomeric across ~401 million molecules

Dhaked, D. K. *et al.* J. Chem. Inf. Model. **2020**, 60, 3, 1253–1275

6

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How does InChI up to version 1.05 handle tautomerism?

- InChI is in principle designed to be tautomer-invariant
- Standard InChI handles a limited range of tautomerism types
- One can turn on additional tautomeric types in non-standard InChI via options: KET, 15T
- It was recognized early on that important types of tautomerism are missing

7

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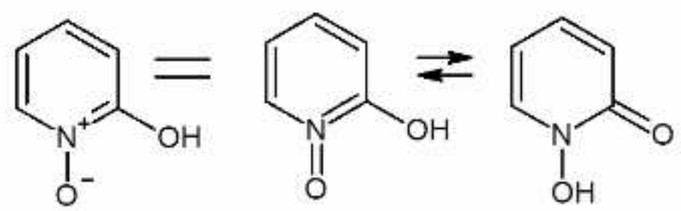
Why a new version of tautomerism handling needed?

Proposal by Dmitrii Tchekhovskoi in 2012:

- Another breaking change:

Add 1,4-oxime/nitroso tautomerism



InChI=1S/C5H5NO2/c7-5-3-1-2-4-6(5)8/h1-4,7H

InChI=1S/C5H5NO2/c7-5-3-1-2-4-6(5)8/h1-4,8H

8

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Rule Set

All rules expressed as SMIRKS, applied in CACTVS

		nn (need not be contiguous)		Number of rules
CACTVS Standard Rules	02–12	Common	New extensions: PT_11_*0m*, *m* = 1 - 4	24
	13–21	Rare		
Prototropic Rules PT_*nn*_*mm* — New Rules	22–49	(includes subrules PT_*nn*_0*m*, *m* > 0)		30
Ring-Chain Rules RC_*nn*_*mm* — New Rules	03–24	← Includes ... rules from ref. (1) (includes subrules RC_*nn*_0*m*, *m* > 0)		54
Valence Tautomerism Rules VT_*nn*_*mm* — New Rules	01–10	(includes subrules VT_*nn*_0*m*, *m* > 0)		11

Total number of rules: 119

(1) Guasch L. *et al.*, J. Chem. Inf. Model. **2014**, 54, 2423−2432
Dhaked D. *et al.*, J. Chem. Inf. Model. **2020**, 60, 3, 1090−1100
Dhaked D. *et al.*, J. Chem. Inf. Model. **2020**, 60, 3, 1253−1275
Dhaked D., Nicklaus M. ChemRxiv 10.26434/chemrxiv.14779254.v1

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Tautomer Enumeration Tool

https://cactus.nci.nih.gov/tautomerizer/

NCI/CADD Group

Tautomerizer - Predict tautomers based on 80+ rules

Introduction | Form | Individual Rule Pages | Rules Sources | Help

Enter the structure in SMILES format

1. Input Structure SMILES: Structure Editor

Submit

2. Single step or Multi step:

Single step ○ Multi step

3. Activate rules:

○ Activate all rules
○ Activate standard rules
○ Activate only new rules
○ Enter your own rule as SMIRKS:
● Activate custom rule set via following checkboxes:

Select rules

☐ PT_02_00 - **1,5 (thio)keto/(thio)enol** - [O,S,Se,Te;X1:1]=[Cz1H0:2][C:5]=[C:6][CX4z0,NX3:3][#1:4]>>[#1:4][O,S,Se,Te;X2:1][Cz1:2]=[C:5][C:6]=[Cz0,N:3]
○ Select example: C1=CC(C=C(C1=O)C)=O
Run Example

☐ PT_03_00 - **simple (aliphatic) imine** - [#1,a,O:5][NX2:1]=[Cz{1-2}:2][CX4R{0-2}:3][#1:4]>>[#1,a,O:5][NX3:1]([#1:4])[Cz:2]=[C:3]
○ Select example: [C]1(CC[C]CC1)=[N]
Run Example

☐ PT_04_00 - **special imine** - [Cz0R0X3:1]([C:5])=[C:2][Nz0:3][#1:4]>>[#1:4][Cz0R0X4:1]([C:5])[c:2]=[nz0:3]
○ Select example: C(CC1=NC=C[NH]1)(C)C
Run Example

10

Hitesh Patel

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Chat

CoV-2 RNA genome is approx. 30.000 bp = around 1.200.000 atoms ☺

Yulia Borodina to Everyone 07:35 PM

@Ulrich

Evan Bolton to Everyone 07:39 PM

Thanks Aleksandr! Yes, one could imagine being able to work with other formatted data. The use cases of InChI for search tend to be focused around near-field 'sameness' .. so the search scheme might partially fill this use case.

Thanks Ulrich! Yes .. there are some really good ones out there .. the PDB has some real large ones these days (ribosomes, etc.).

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InChI[Key] (V. 105) only Partially Recapitulates a More Complete Set of Rules

InChI Calculation Type >		Standard	(DONOTADDH W0)	
Database	Database Size	Tautomeric Part	InChI Success Rate (%)	Strict InChI Success Rate (%)
CSD	319,201	203,108	26.25	13.46
ChEMBL	1,820,035	1,578,290	62.15	28.55
AMS	8,409,644	7,204,965	64.77	29.85
PUBCHEM	96,502,282	78,807,315	56.64	29.47
CSDB	141,743,903	127,543,398	71.27	31.90

Rules applied in chemoinformatics toolkit CACTVS

Devendra Dhaked

InChI Calculation Type >		Non-standard	(DONOTADDH W0 RECMET NEWPS SPXYZ SAsXYZ Fb Fnud KET 15T)	
Database	Database Size	Tautomeric Part	InChI Success Rate (%)	Strict InChI Success Rate (%)
CSD	319,201	203,108	48.83	30.90
ChEMBL	1,820,035	1,578,290	73.91	37.46
AMS	8,409,644	7,204,965	71.99	36.32
PUBCHEM	96,502,282	78,807,315	66.52	38.26
CSDB	141,743,903	127,543,398	78.70	38.97

Dhaked D. *et al.*, J. Chem. Inf. Model. **2020**, 60, 3, 1253–1275

InChI Success Rate: At least two rule-enumerated tautomers have same InChIKey

Strict InChI Success Rate: **All** rule-enumerated tautomers have same InChIKey

11

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Ulrich Schatzschneider to Everyone 07:46 PM

How fixed are these rules? Are they "hard-coded" into the main code and need a lot of effort to add/modify or is there another more low-key mechanism to append in case further exceptions are identified?

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New Rules: Integrated in experimental version of InChI 1.06

- New rules, as implemented in CACTVS, expressed as SMIRKS
- InChI doesn't have a SMIRKS parser
- Adding new tautomeric rules requires **code changes in the core of InChI**

- We picked ~20 prototropic rules as candidates for implementation in InChI
- No ring-chain or valence tautomerism rules – impossible to add to current InChI

- Igor Filippov was able to add **six new rules**

Note: These were all the rules that could be added; for others, the effort was unsuccessful!

Igor Filippov

Six new rules implemented in InChI library (based on V. 1.06 code) integrated in CACTVS.

Wolf-D. Ihlenfeldt

12

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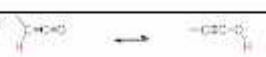
New Rules Implemented

PT_06_00	 1,3 heteroatom H shift	[CX{2-3}r{0-1}:N,n,S,s,O,o,Se,Te:1]-[NX2,nX2,CX1,c,P,p:2][N,n,S,O,Se,Te:3][#1:4] >>[#1:4][CX3r{0-1}:N,n,S,O,Se,Te:1][NX2,nX2,CX3r{0-1},c,P,p:2]-[N,n,S,s,O,o,Se,Te:3]
PT_13_00	 ketone-enol exchange	[O,S,Se,Te;X1:1]-[C:2]-[C:3][#1:4]>>[#1:4][O,S,Se,Te;X2:1][C:2]=[C:3]
PT_16_00	 nitroso/oxime	[#1,1][O,R:2][N+0,r3]=[CX3,4]>>[O,R:2]-[N+0,r3][CX4,4][#1,1]
PT_18_00	 cyanic/iso cyanic acids	[#1:1][O:2][C:3]-[N:4]>>[O:2]=[C:3]=[N:4][#1:1]
PT_22_00	 imine/imine	[#1,1][CX4,2][NX2,3]-[CX3,4]>>[CX3,2]-[NX2,3][CX4,4][#1,1]
PT_39_00	 nitrone/oxaziridine Beckmann rearrangement	[CX3,NX2:1]=[NX3+:2][O-:3].[CX4:4][#1:5]>>[#1:5][CX4,NX3:1][NX3+:2][O-:3]-[CX3:4]

Note that example structures are just that: examples. Similar for the names. The SMIRKS are really defining the rule!

In InChI, new code has to be written!

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The problem at least in inorganic compounds for almost everything is "the rule is there is no general rule"

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What have we gained with the six new rules?

Total of 8 rules: KET, 15T, PT_06_00, PT_13_00, PT_16_00, PT_18_00, PT_22_00, PT_39_00

Counting various identifiers for recent version of PubChem (2020-02 Compound database):

90,600,000 compounds analyzed for the PubChem file(s)

Number of cases where S, N, T same:	26,339,099
Number of cases where S, N same, T diff:	28,104,489
Number of cases where N, T same, S diff:	10,892,602
Number of cases where S, N, T diff:	25,252,306

Note: Most analyses were done with InChKeys but could as well have been done with InChIs

90,390,917 unique Standard InChIKeys found

87,322,470 unique non-standard InChIKeys (with KET and 15T turned on)
87,322,472 unique Tauto InChIKeys with KET and 15T turned on

Differences vs. the non-standard InChIKey count:

84,249,356 (-3.519%, -3,073,114) unique Tauto InChIKeys (with all 8 rules turned on)

87,448,002 (0.144%, 125,532) unique Tauto InChIKeys with just KET turned on
90,184,001 (3.277%, 2,861,531) unique Tauto InChIKeys with just 15T turned on
86,004,390 (-1.509%, -1,318,080) unique Tauto InChIKeys with just PT_06_00 turned on
90,310,034 (3.421%, 2,987,564) unique Tauto InChIKeys with just PT_13_00 turned on
90,284,657 (3.392%, 2,962,187) unique Tauto InChIKeys with just PT_16_00 turned on
90,326,333 (3.440%, 3,003,863) unique Tauto InChIKeys with just PT_18_00 turned on
88,785,161 (1.675%, 1,462,691) unique Tauto InChIKeys with just PT_22_00 turned on
90,324,463 (3.438%, 3,001,993) unique Tauto InChIKeys with just PT_39_00 turned on

14

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Tautomer Structures Extracted from Experimental Literature: "Tautomer Database"

https://cactus.nci.nih.gov/download/tautomer/

Release 3 - November 2019

2,819 Tautomeric Tuples Comprising 5,977 Structures

Structurally different tuples: 1,776 (comprising **3,884 different structures**)
since some tuples are differentiated from each other only by experimental conditions such as solvent, spectroscopy method, etc.

See https://doi.org/10.1021/acs.jcim.9b01156
and https://doi.org/10.26434/chemrxiv.10790369.v1 for literature about this database.

Dhaked D. *et al.*, J. Chem. Inf. Model. **2020**, 60, 3, 1090–1100

15

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Hunter Moseley to Everyone 07:50 PM

Does CACTUS parse SMIRKS rules every time or are they pre-parsed and saved in compilable or actionable form?

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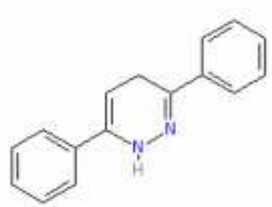
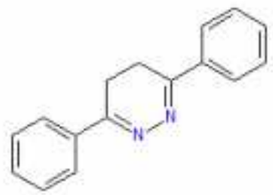
Only Tauto InChI Identifies Tautomers





Non-standard InChIKey:	UHFJDRXFXQDUHB-UHFFFAOYNA-N	GEHJYGJMMCSVQL-UHFFFAOYNA-N
Tauto InChIKey:	YAMMWMQCRXUUCQ-UHFFFAOYNA-N	YAMMWMQCRXUUCQ-UHFFFAOYNA-N

Case: 115_01 and _02

19

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On PubChem: keep in mind that a good part of the inorganic structures is more or less nonsense due to "disconnection" - for example has cisplatin and transplatin as "synonyms" although cisplatin is a multibillion dollar anticancer drug while transplatin is inactive. Same with ferrocenes important in catalysis

Jonathan Goodman to Everyone 07:53 PM

Why does the tautomer code have to be in the core InChI? It seems an ideal post-processing step: does this Standard InChI have another tautomeric form and, if so, which one is preferred?

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Summary

Compared with a comprehensive set of tautomeric rules:

- Current Standard InChI recapitulates ~30% of amenable compounds
- Current Non-Standard InChI (KET, 15T) recapitulates ~37% of compounds
- Relative to Standard InChI, Non-Standard InChI (KET, 15T) equates 3.5% more compounds as tautomers of other compounds in a typical large database (e.g. PubChem)

Working group achievements:

- Six new prototropic rules were added to InChI code
- Relative to Standard InChI, "Tauto InChI" (KET, 15T, 6 new rules) equates 7% more compounds as tautomers of other compounds, i.e. yet 3.5% more than Non-Standard InChI

Availability:

- Experimental version of InChI 1.06 released with 6 rules added

21

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Conclusion

Notes and Questions:

- **Tauto InChI is different InChI: many InChIKeys are different. Do not mix with non-standard InChI!**
- Maybe should have kind indicator "T" instead of "N": **WCHQBIYPPGCACF-UHFFFAOYTA-N** ?

- How to test: Which rules are realistic, which ones may be too strict?

Future outlook:
- Prototropic transforms: doubtful whether more can be added
- Ring-chain, valence tautomerism: likely incompatible with current InChI chemical structure model

- **To be able to add more rules, InChI code likely needs to be re-written**

22

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and saved in compilable or actionable form?

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What if different tautomers can be stabilized under different conditions - wouldn't selection of a preferred one then case problems as they have to be distinguished?

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Acknowledgements

Markus Sitzmann
Waruna Yapamudiyansel
Megan L. Peach
James A. Kelley
Joseph J. Barchi
Jeff Saxe
Igor Filippov

Members of the IUPAC Working Group:
Gerd Blanke
Evan Bolton
Alex M. Clark
Bret Daniel
Devendra Dhaked
Laura Guasch
Wolf-Dietrich Ihlenfeldt
Gregory Landrum
John W. Mayfield
Hitesh Patel
Roger Sayle
Dmitrii Tchekhovskoi

Igor Pletnev (†)

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FDA | OFFICE OF DATA, ANALYTICS, AND RESEARCH

Challenge announcement

FDA plans to open a public challenge in collaboration with the InChI Trust and IUPAC Working Group on tautomers

Challenge title (tentative): Crowdsourced evaluation of InChI-based tautomer identification

Timeframe (tentative): September 2022 – January 2023

Purpose: Determine how well InChI algorithm agrees with experimental determination of tautomers in chemical databases

Why it Matters: Tautomers are molecules that interconvert at normal conditions and should therefore be considered the same substance for the purpose of regulation of their therapeutic use and/or tracing their presence as impurities in products

Incentives for participants:

- Recognition by FDA as participant in helping to enable improvements in health outcomes
- Opportunity to co-author a paper

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There is also the issue of knowing the energy barrier in the solvent of interest

If you can put the tautomer in the bottle (and it does not scramble quickly, say seconds, then it may be important .not. to collapse?)

Me to Everyone 08:02 PM

@Ulrich Check the different Smiles/ non-standard InChI about 2-hydroxy pyridine/2-pyridone e.g. on https://en.wikipedia.org/wiki/2-Pyridone

Ulrich Schatzschneider to Everyone 08:02 PM

Does the barrier really matter? It's again "outside Information". Isn't it enough that a person preparing a structure thinks it is sufficiently different from something else that it should be differentated?

Me to Everyone 08:02 PM

The interchange may be dynamic (solution), or frozen (e.g., solid state/ crystal).

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Challenge Background:

- Since 2010, the InChI Trust has supported the continual development of a standard way to encode molecular information and to facilitate the search for such information in databases and on the web
- The InChI identifier is computed from chemical structure and is not sensitive to certain variations of structure representations.
- However, it doesn't recognize some cases of structures being tautomers of each other.
- Tautomer Working Group suggested a few modifications to the InChI algorithm that would recognize more tautomer types

Challenge Objectives:

- Members of Industry, Government, and Academia will be invited to test the InChI algorithm modifications on their real chemical samples by:
  1. Running their database of structures through specified computational analyses
  2. Comparing identified tautomeric sets with their internal analytical data, most likely NMR spectroscopy
  3. Determining whether members of these sets can interconvert at normal conditions
  4. Reporting the summaries of their analyses for tautomeric rule sets
- As a result, participants will:
  - Help with the creation of better tautomer-invariant identifiers
  - Find previously unknown tautomeric duplicates in their databases

5

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Evan Bolton to Everyone 08:03 PM

If you can separate it in the bottle and do separate chemistry on it .. yes, it matters very much to be able to associated data to it separately

Marc Nicklaus to Everyone 08:03 PM

@Jonathan: Yes, it would make things much easier if (s0me part of) the tautomerism part of InChI V2 would not be in the very core of the code. But in V1 it is.

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rudy potenzone | Mick Kappler | Mick Kappler | Yulia Borodina

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What is precisionFDA?

https://precision.fda.gov

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Ulrich Schatzschneider to Everyone 08:06 PM

In a "hydrogen-pruned" version of a structure tautomers will get the same identifier (prune = non-bridging H completely removed/ignored) ...

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rudy potenzone

Mick Kappler

Mick Kappler

Yulia Borodina

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A secure, collaborative, high-performance computing platform that builds a community of experts around the analysis of biological datasets in order to advance precision medicine.

EXPERT HIGHLIGHT

New Tools: Processing Electronic H ... and Increasing Potential Adverse Ev...

Roselie A. Bright, ScD, MS and Summer R...

Most clinical safety systems, including ... and patients, despite well-documentr... condition is reportable, and burden... true authorship of literature writt... notice the approaching army, des...

Expert Q&A ☆ About Th...

6,000+ Users
107 Terabytes of Data
136 Unique Publicly Available Apps
31 Challenges
Cited in a Total of 78 Scientific Publications
11 Contributed/Written Scientific Publications
21 Training Videos
5 Training Workshops

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UPCOMING CHALLENGES

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Chat

Ulrich Schatzschneider to Everyone 08:06 PM

In a "hydrogen-pruned" version of a structure tautomers will get the same identifier (prune = non-bridging H completely removed/ignored) ...

Thomas Doerner to Everyone 08:07 PM

Re. interconverting and not interconverting tautomers: Would the combination of a very fine-grained identifier part (no tautomer merging) plus an aggregation part which aggregates different tautomers (to aid finding tautomers) as an overall InChI address the various needs ? (the members of the organometallics InChI team may remember this kind of proposal... :-)

Marc Nicklaus to Everyone 08:07 PM

@Daniel: Since I did this analysis in CACTVS. I don't think I saw a difference in speed when the 6 rules were added. But running the InChI library within CACTVS is generally significantly slower than the stand-alone InChI executable.

Who can see your messages?

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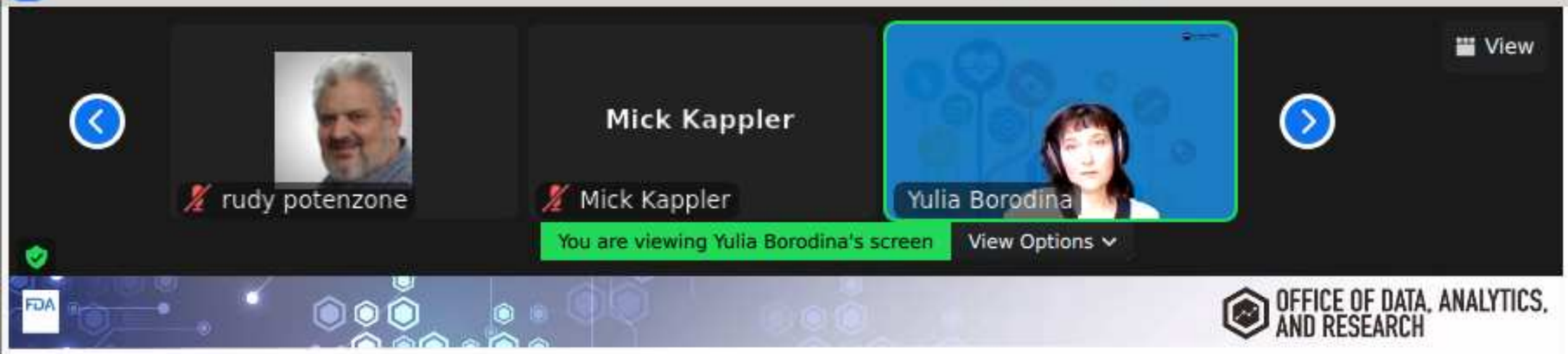

Data on pFDA are secure and private unless shared

- All data brought to precisionFDA are private by default, cannot be viewed by anyone else
- One can use public apps with private data
- Adding files to precisionFDA:
  - Upload through web UI under My Home->Files
  - Upload from command line with pFDA command line uploader https://precisionfda-staging.dnanexus.com/docs/files#files-uploading
  - Import from a public URL via the URL Fetch app

10

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rudy potenzone | Mick Kappler | Yulia Borodina

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Tautomeric rule sets for testing

1-rule-sets:

- KET: keto-enol tautomerism recognized
- 15T: 1,5 H-transfer recognized
- PT_06_00: "1,3 heteroatom H shift" recognized
- PT_13_00: "keten/ynol exchange" recognized
- PT_16_00: "nitroso/oxime" tautomerism recognized
- PT_18_00: "cyanic/iso-cyanic acids" tautomerism recognized
- PT_22_00: "imine via imine" tautomerism recognized
- PT_39_00: "nitrone/azoxy or Behrend rearrangement" recognized

2-rule-set:

- KET + 15T

5-rule-set:

- PT_13_00+PT_16_00+PT_18_00+PT_22_00+PT_39_00

6-rule-set:

- PT_06_00+PT_13_00+PT_16_00+PT_18_00+PT_22_00+PT_39_00

7-rule-set:

- 15T+PT_06_00+PT_13_00+PT_16_00+PT_18_00+PT_22_00+PT_39_00

8-rule-set:

- KET+15T+PT_06_00+PT_13_00+PT_16_00+PT_18_00+PT_22_00+PT_39_00

13

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@Thomas: Good to bring this up again - I think the issue of how finely "grained" an identifier should be still seems to be unclear ...

Andrey Yerin to Everyone 08:09 PM

I would say that tautomer module can be in 'preparation' module. There one 'best taut' can be created and in this way tauts will have the same InChI. While may need format changes - no need to idicate distributed location of H

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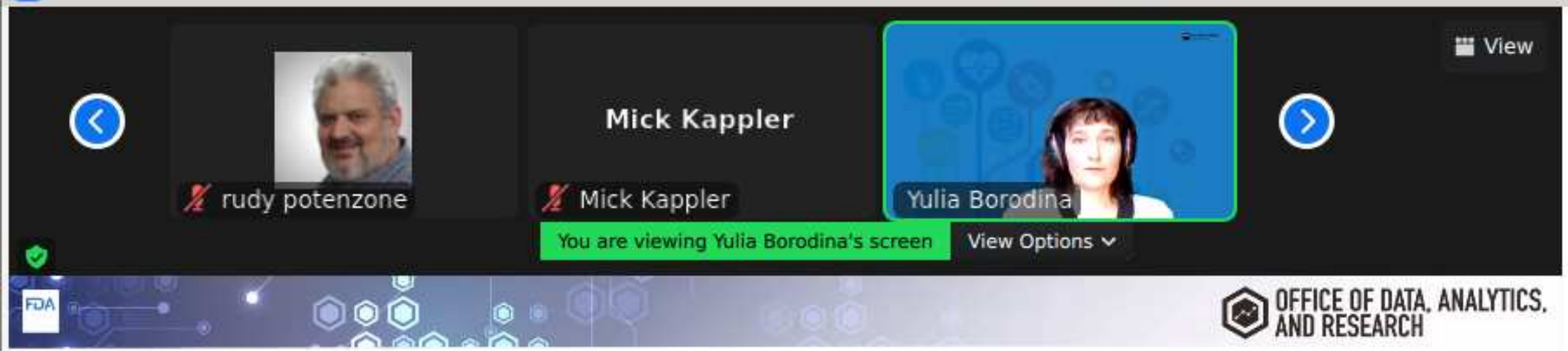

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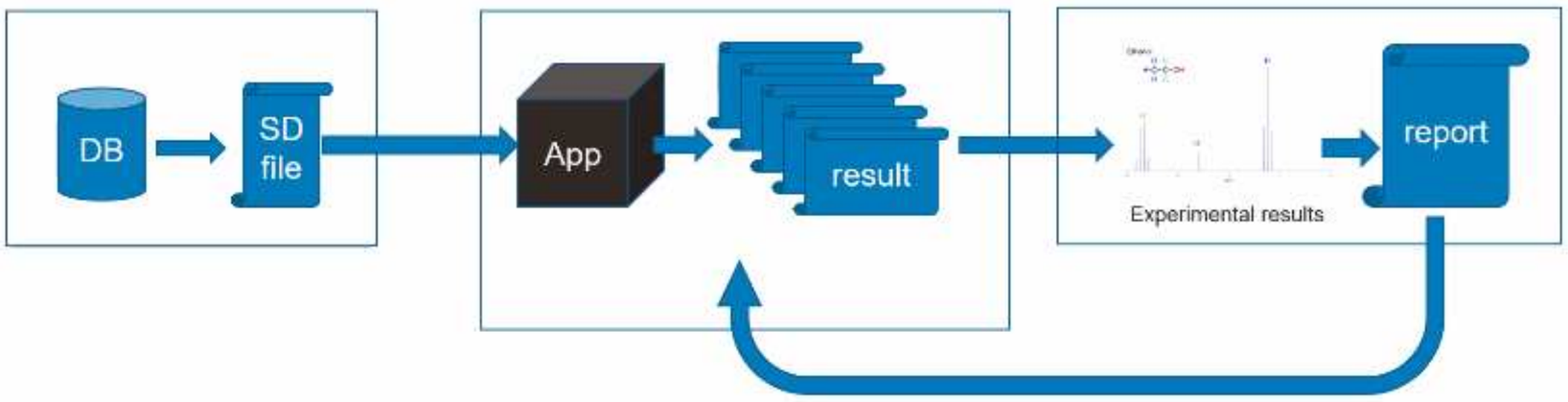
Zoom Meeting

Workflow 1 – For participants who can upload files with structures

Participant site | precisionFDA platform | Participant site



14

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Ulrich Schatzschneider to Everyone 08:10 PM

For a regulatory person or sombody who wants to order a commercial compound "can be put in a bottle" is enough - if one needs to identify something in an ELN, it might be different depending on your type of chemistry. Not everybody is a synthetic chemist - think low-temperature spectroscopists or gas phase mass spectrometry people - all of them also ned identifiers!

Marc Nicklaus to Everyone 08:10 PM

@Ulrich and Evan: I think repository managers would be interested in knowing if molecules can tautomerically interconvert within, say, months. But this is part of the larger discussion of what the foremost use case of InChI should be.

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Interested in participating?

Contact yulia.borodina@fda.hhs.gov

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attached reference I already thought so: Evolution of Novartis' Small Molecule Screening Deck Design https://doi.org/10.1021/acs.jmedchem.0c01332

Me to Everyone 08:15 PM

@Marc But what often happens is that you one hasn't one .or. the other , but one preferentially over the other (i.e., a blend). Cf. Tautobase, https://github.com/WahlOya/Tautobase

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@Hinnerk Problem is how many applications actually use "non-standard InChI" or at least allow you to switch between "standard" and "non-standard"? If non-standard is there but not use beyond small developer community it is almost as good as not there at all (= not of help)

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@Ulrich: Absolutely, in out Tautomer Database we see "blends" very frequently, just like in Tautobase.

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rudy potenzone

Mick Kappler

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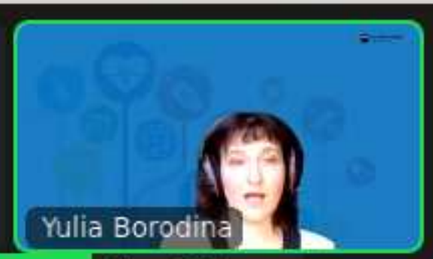

Yulia Borodina

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Acknowledgments

Igor Pletnev (InChI Trust)
Steve Heller (InChI Trust)
Rudy Potenzone (InChI Trust)
Gerd Blanke (InChI Trust)
Marc Nicklaus (IUPAC WG on tautomers)
Wolf-Deitrich Ihlendfeldt (IUPAC WG on tautomers)
Andrey Yerin (ACDlabs)
Antony Williams (EPA)
Charles Lowe (EPA)
Lutz Weber (Ontochem)
Mitch Miller (Scientific Thinking LLC)
Yurii Moroz (Enamine)
Yuri Pevzner (Abbvie)

Elaine Johanson (FDA)
Annette Vernon (FDA)
Letria Hall (FDA)
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24

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