Exemplified Compounds Table linked to Citing Publications

A structure summary report

Maddy Marley
Senior Information Scientist
Global Patents
GSK

GSK Information Science colleagues worldwide

*……..serving the global attorney community*

Chemistry structure reports

– Produced by the chemistry information scientists for attorneys

– Enable attorneys to strategically draft their patent applications and discover/overcome any FTO hurdles

– Enable attorneys to achieve **best possible protection** for GSK's products

    i.e. valid and enforceable patents

– Support the Pharma and Consumer businesses

    – **2017 Annual report:**

        – **Pharmaceuticals turnover: £17.3bn +7% AER, +3% CER (57% of Group turnover)**

        – **Consumer Healthcare turnover: £7.8bn +8% AER, +2% CER (26% of Group turnover)**

Chemistry Reports

– Discovery/pre-candidate/candidate selections

  – Patentability

    – Compounds within Markush

    – Compounds peripheral to Markush + similar use

    – Any source, anywhere. Include proprietary databases

– First time in Human, Commit to Medicine Development, Commit to Phase 3

  – Freedom-to-operate

    – Narrow genus around the candidate structure or process intermediates

    – Patent claims, patents in-force or pending

– Validity

  – A date-ranged patentability
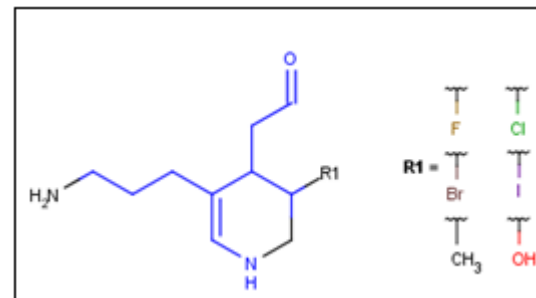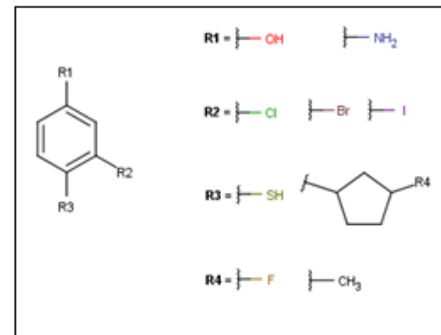
Attorney feedback on reports

- **In order to clearly analyse <u>the compounds</u> of interest:**
  - Present them in a table
  - No duplicates
  - <u>**Link**</u> the compounds to the references
- **In order to view the references**
  - Provide at least one family member, containing the structures ("basic")
  - Provide the journal source
- **Reports delivered in a WORD document**
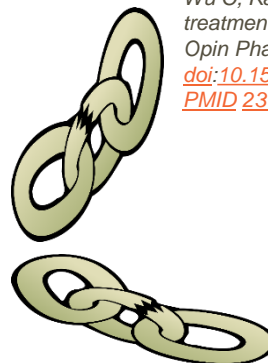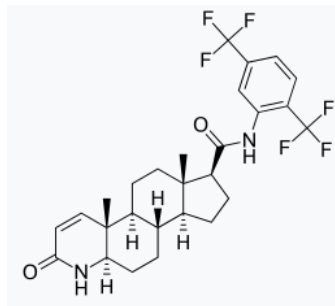
*Wu C, Kapoor A (2013). "Dutasteride for the treatment of benign prostatic hyperplasia". Expert Opin Pharmacother. **14** (10): 1399–408. doi:10.1517/14656566.2013.797965. PMID 23750593.*

An oral pharmaceutical composition of dutasteride

EP 2395975

Sources used for Chemistry reports:

- Chemical Abstracts on New STN, STN Classic, STNext
  - Compounds found here are the crown jewels or crown of thorns
- DWPI
- Reaxys Desktop
  - Covers PubChem, EMolecules and other substance collections
- Virtual libraries
  - Zinc, Enamine Real,
- If Validity
  - In addition to above, maybe open-source journals, keyword strings in full-text, patent databases offering name->structure tools, ChemSpider etc.
 - Must be able to "date stamp" the retrieval (open sources can be unreliable)

Focus on Chemical Abstracts Registry/CA files

– *Reporting Option 1: "BIB ABS HITSTR"*

– If hit structures belong to >1 reference they are repeat displayed

– Compounds that are mixtures are space-consuming

– Split page–compounds are sometimes undecipherable

3-Pyridinecarboxamide, 6-(1-pyrrolidinyl)-N-[4-[[3-[[5-
(trifluoromethyl)-2- pyridinyl]oxy]phenyl]methylene]cyclohexyl]-
(CA INDEX NAME)

PAGE 1-A

PAGE 2-A

NO GO!
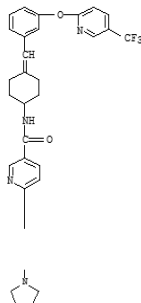
```
AN    2017:1847128  HCAPLUS  Full-text
TI    Crystallization of bisulfite derivatives of enantiomerically enriched
      verbenone
AU    Kovalenko, V. N.; Prat'ko, A. S.; Prokhorevich, K. N.
CS    Belarusian State University, Minsk, 220030, Belarus
SO    Russian Journal of Organic Chemistry (2017), 53(10), 1598-1600
      CODEN: RJOCEQ; ISSN: 1070-4280
DOI   10.1134/S1070428017100190
PB    Pleiades Publishing, Ltd.
DT    Journal; (online computer file)
LA    English
AB    After sepn. of cryst. bisulfite derivs. of enantiomerically enriched (1S)-
      and (1R)-verbenones, steam distn. of the filtrates afforded (1S)- and
      (1R)-verbenones whose optical purity was higher by 30 and 20%, resp., than
      that of the initial enantiomers.

      CM    1

      CRN   7631-90-5
      CMF   H2 O3 S . Na
```

```
      CM    2

      CRN   80-57-9
      CMF   C10 H14 O
```

```
RE.CNT  3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

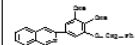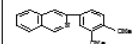# Focus on Chemical Abstracts Registry/CA files

– *Reporting Option 2 -* TABLE TOOL (STN Express)

– Impossible to fit-to-size in a report without losing legibility

– Patents and non-patent records mixed together resulting in empty cells

– Hit structures repeat-displayed

Title	Patent Information					Source	Patent Assignee/Corporate Source	Hit Structure
One substrate, two modes of C-H functionalization: a metal-controlled site-selectivity switch in C-H arylation reactions						Organic Letters (2017), 19(1), 262-265 CODEN: ORLEF7; ISSN: 1523-7052	Department of Chemistry, Indian Institute of Science Education and Research Bhopal, Madhya Pradesh, 462066, India	CAS Registry Number 67237-89-2 HCAPLUS Chemical or Trade Name Isoquinoline, 3-(3,4-dimeth INDEX NAME)
Antimicrobial agents	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	U.S., No pp. given CODEN: USXXAM	Rugers, The State University of New Jersey, USA; University of Medicine and Dentistry of New Jersey; Rutgers, The State University of New Jersey	CAS Registry Number 1352036-15-7 HCAPLUS Chemical or Trade Name Isoquinoline, 3-[3,4-dimethoxy-5-(phenylm (CA INDEX NAME)
	US 8933096	B2	20150113	US 2012-137029 36	20121207			CAS Registry Number 1352036-40-8 HCAPLUS

Focus on Chemical Abstracts Registry/CA files

– *Reporting Option 3 New STN, Excel output*

- Lots of editing necessary – no saveable custom display format

- Does not overcome repeat-displaying the structures

- The All Hit Structures link doesn't work in a Word document

    - Unless you "associate" the file containing the structures- this becomes awkward

Title	Hit Structure Images
Crystallization of bisulfite derivatives of enantiomerically enriched verbenone	All Hit Structures
Preparation of secondary amide quaternary ammonium salt-type hydroxypropyl sodium sulfonate as asphalt emulsifier	All Hit Structures

Enter an IT genius

Maz's Macro

```
        Call IAFunctions.RestoreSettings2(mMyInfo)
        Call IAFunctions.ClearSelectionObject(True)

        MsgBox "Error! Details of the error follow. The macro will then terminate." _
        & vbCrLf & vbCrLf _
        & "Error: " & vbTab & errNumber & vbCrLf _
        & "Where: " & vbTab & errSource & vbCrLf _
        & "What: " & vbTab & errDescription & vbCrLf & vbCrLf _
        & "" _
        , vbCritical, mcsAppName
        On Error Resume Next
        Unload frmExCTF_Progress
        Exit Sub
    End Sub


    Sub ExCTF2(dummy As Variant)
        'called by the Activate event of frmExCTF_Progress
        'all errors bubbled up to sub ExCmpdTableFormatter from here on

        Const RefAboveTitle As String = "Reference "
        Const ReferencesBookmarkPrefix As String = "Ref"
        Const CompNumberBookmarkPrefix As String = "CompNum"
        Const CompNumPrefix As String = "Compd."
        Const graphicPlaceholder As String = "XX"
        Const STNPromptCharacter As String = "->"

        On Error GoTo errh

        Dim bMiscDataExists As Boolean
        Dim PlaceHolderRange As Range
        Dim ResultsTable As Range
```
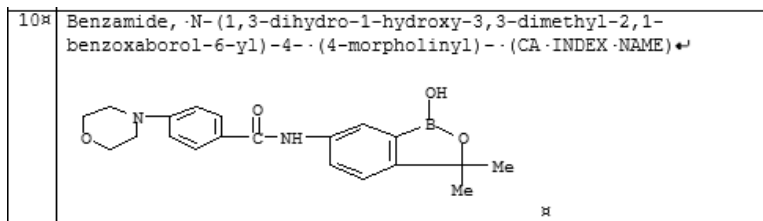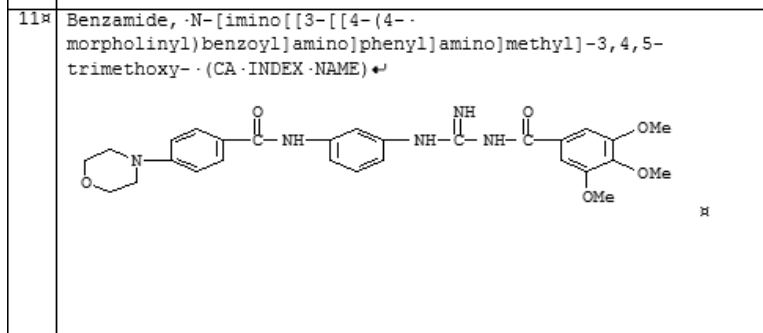
10¤	Benzamide, ·N-(1,3-dihydro-1-hydroxy-3,3-dimethyl-2,1-benzoxaborol-6-yl)-4-·(4-morpholinyl)-·(CA·INDEX·NAME)↵	•→ preparation ·of· benzoxaborole ·mols. as ·antiprotozoal· agents ·useful ·in· the ·treatment ·of· protozoal ·infection· Reference ·- ·2¶
11¤	Benzamide, ·N-[imino[[3-[[4-(4-·morpholinyl)benzoyl]amino]phenyl]amino]methyl]-3,4,5-trimethoxy-·(CA·INDEX·NAME)↵	•→ drug ·candidate; · preparation ·of· acylguanidines ·as· inhibitors ·of· Hedgehog ·protein· signalling ·pathway· for ·treatment ·of· ca... neu... dis... dia... - ·...
12¤	2-Pyridinecarboxamide, ·N-[3-(2-amino-5,6-dihydro-4-methyl-4H-1,3-thiazin-4-·yl)phenyl]-5-(4-morpholinyl)-·(CA·INDEX·NAME)↵	•→ pro... tre... Alz... Ref...

Fulltext link for patents and non-patents

Reference 2

```
TI    Preparation of benzoxaborole molecules as antiprotozoal agents and
      their use in the treatment of protozoal infection
AN    2011:200035 HCAPLUS   Full-text
DN    154:259801
IN    Chen, Daitao; Orr, Matthew; Sligar, Jessica; Jacobs, Robert; Plattner,
      Jacob J.
PA    Anacor Pharmaceuticals, Inc., USA
SO    PCT Int. Appl., 202pp. CODEN: PIXXD2
DT    Patent
LA    English
PI    WO 2011019618 A1 20110217 WO 2010-US44787 20100806
PRAI  US 2009-61234213 P 20090814 US 2010-61315774 P 20100319 WO 2010-US44787 W
      20100806
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS    CASREACT 154:259801; MARPAT 154:259801GI
```
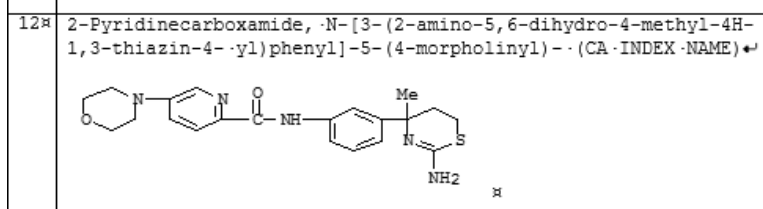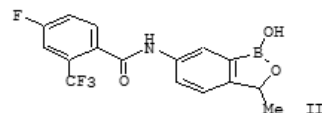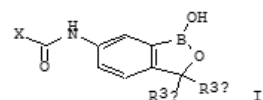


```
IT    1266120-43-7P [Compd.10] RL: ADV (Adverse effect, including toxicity); PAC
      (Pharmacological   activity);   PKT   (Pharmacokinetics);   SPN   (Synthetic
      preparation);   THU   (Therapeutic   use);   BIOL   (Biological   study);   PREP
      (Preparation);   USES   (Uses)   (preparation   of   benzoxaborole   mols.   as
      antiprotozoal   agents   useful   in   the   treatment   of   protozoal   infection)
              COPYRIGHT ACS
```

Maz's macro – enables clients to clearly analyse the exemplified compounds –GOAL!

– Runs in Word

– Produces a Table of Compounds from the BIB ABS HITSTR display (STN Express, STNext)

  – No duplicates

– Each compound contains hyperlink(s) to references (s)

– References are in BIB ABS HITIND format, in underneath the table

– Each CASRN in the reference is hyperlinked back to the table compound
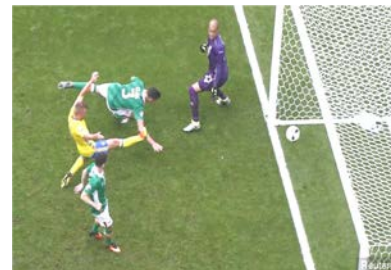
– **BUT**

  – Macro written in 2001 for Word 97 – still in use today! (Word 2016)

  – It is very tricky to install, and often falls over

  – Still a problem with large structures (pg1a/pg2a) and references look "old-fashioned"

  – Does not work at all for New STN output

  – GSK needed to seek long-term solution to move forward with post-processing

Enter BizInt!

BizInt Smart Charts
Software for Business Intelligence

– Post-search processing market leader

– Highly respected and influential to patent information professionals

– Long-standing relationship with GSK of >10yrs, small organisation, trustworthy, good at listening

– Patent/Non-Patent Smart Charts extensively used in the GP information team, robust product

    – Changes we have requested in the past (example, with Orbit output) have been implemented quickly

– Experienced with STN, (and all its platforms**!)** and with working together with database providers

– Strong track record for providing post processing solution from many applications/platforms.

– BizInt is an export option in many databases including those key to our work:

    – STN Express/STNext

    – New STN

    – Orbit

    – Cortellis

– BizInt Reference Rows allows merging of the "best" features of databases into one row

    – Orbit patent family legal status and claims with Chemical Abstracts structure displays

– Tables can be updated with new references

BizInt – Initial Release March 2018 New STN

Software for Business Intelligence

BizInt Smart Charts

L4 (2158317-14-5 OR 2159095-42-6 OR 2160562-95-6 OR 2160606-03-9 OR 2160606-04-0 OR 2161401-82-5)/rn
CAplus, REGISTRY

CAplus	5
REGISTRY	6

C:\Users\MAM70206\Desktop\BIZINT\test3.chp

Combined: refs

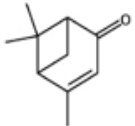|	Title	Patent Assignee	Abstract	Source	Patent Family			Graphic Information	Priority Date
					Patent	Kind	Date		
3	Compounds and methods for treating bacterial infections	Washington University, United States (US)	The present invention encompasses compds. and methods for treating and preventing bacterial infections specifically urinary tract infections and those caused by bacteria contg. type 1 pili present invention encompasses c methods for trea bowel disease s Disease.	PCT Int. Appl. PIXXD2, pp. 175	CA2913622	A1	20141204		2013-05-30
					WO2014194270	A1	20141204		
					AU2014273962	A1	20151217		
					EP3003322	A1	20160413		
					CN105682665	A	20160615		
4	Compounds and methods for treating bacterial infections	The Washington University, United States (US)	The invention en mannoside com for treating urina						
5	Mannoside compounds for treating Urinary tract bacterial infections	The Washington University, United States (US)	The present inve encompasses c methods for trea infections.						

Display Columns

Available Columns

- Accession Number
- Application Details
- Basic Patent Number
- CA Classification
- CA Doc Type
- CPC
- BizInt Database
- Dates
- Designated States
- DOI
- ECLA Class
- Entry Date
- Hit Index Terms
- Hit Registry Numbers
- Index Terms
- International Patent Class
- Inventor(s)
- Language

Selected Columns

- Title
- Patent Assignee
- Abstract
- Source
- Patent Family
- Graphic Information
- Priority Date

>   >>   <   <<

Up   Down

BizInt – Initial Release March

	Substance	Structure	Reference
1	2161401-82-5 Sulfurous acid, compounds, sodium salt, compd. with 4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-one (1:1:1)	CM1 CRN 7631-90-5 • Na CM2 CRN 80-57-9	crystn. of bisulfite derivs. of enantiomerically enriched verbenone *Reference 1*
2	2160562-95-6 1-Octadecanaminium, N,N-bis[3-[(hydroxymethyl)amino]-3-oxopropyl]-N-(2-hydroxy-3-sulfopropyl)-, chloride, sodium salt (1:1:1)	• Cl⁻ • Na	prepn. of secondary amide quaternary ammonium salt-type hydroxypropyl sodium sulfonate as asphalt emulsifier *Reference 2*
3	2158317-14-5 Index name not yet assigned	CM1 CRN 95737-68-1 CM2 CRN 29547-00-0	tank-mixed insecticide controlling pest in rice field *Reference 3*

2.

Title: **Antivirulence C-Mannosides as Antibiotic-Sparing, Oral Therapeutics for Urinary Tract Infections**

Corporate Source: Missouri United States

Abstract: Gram-neg. uropathogenic Escherichia coli (UPEC) bacteria are a causative pathogen of urinary tract infections (UTIs). Previously developed antivirulence inhibitors of the type 1 pilus adhesin, FimH, demonstrated oral activity in animal models of UTI but were found to have limited compd. exposure due to the metabolic instability of the O-glycosidic bond (O-mannosides). Herein, we disclose that compds. having the O-glycosidic bond replaced with potency. This new class of C-mannoside antagonists have significantly increased compd. exposure and, as a result, enhanced efficacy in mouse models of acute and chronic UTI.

Source: Journal of Medicinal Chemistry (20161027) Vol. 59, No. 20, CODEN: JMCMAR, ISSN: 0022-2623, pp. 9390-9408
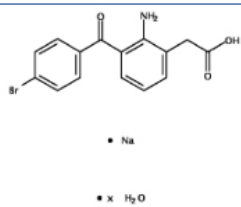
Hyperlinks: **https://pubs.acs.org/doi/abs/10.1021/acs.jmedchem.6b00948**

Notes
Not seen in previous searches

Index Terms:

1393671-31-2P (Cmpd. 38) 1393671-45-8P (Cmpd. 39) 1639335-16-2P (Cmpd. 40) 1639335-26-4P (Cmpd. 41) 2018335-56-1P (Cmpd. 1) 2018335-58-3P (Cmpd. 2) 2018335-62-9P (Cmpd. 3) 2018335-63-0P (Cmpd. 4) Biological Study (BIOL); Pharmacokinetics (PKT); Pharmacological Activity (PAC); Preparation (PREP); Synthetic Preparation (SPN); Therapeutic Use (THU); Uses (USES) (anti-virulence C-mannosides as antibiotic-sparing, oral therapeutics for urinary tract infections)

BizInt – Initial Release March

– Structures can be referenced to one or multiple patents or non patents, along with the context in the document (CAS indexing)

6	2159095-42-6		
	Benzeneacetic acid, 2-amino-3-(4-bromobenzoyl)-, sodium salt, hydrate (1:1:?)	[structure: • Na • x H₂O]	heptamethine cyanine fluorescent dye and application in precise diagnosis and treatment of tumor *Reference 4* observation on the availability and tolerance of 0.1% bromfenac sodium hydrate ophthalmic soln. in the partial substitution of glucocorticoid after LASEK *Reference 5*

-And the CAS RNs in the indexing of the document hyperlink back to the table

Index Terms:

1393671-31-2P (Cmpd. 38) 1393671-45-8P (Cmpd. 39) 1639335-16-2P (Cmpd. 40) 1639335-26-4P (Cmpd. 41) 2018335-56-1P (Cmpd. 1) 2018335-58-3P (Cmpd. 2) 2018335-62-9P (Cmpd. 3) 2018335-63-0P (Cmpd. 4) Biological Study (BIOL); Pharmacokinetics (PKT); Pharmacological Activity (PAC); Preparation (PREP); Synthetic Preparation (SPN); Therapeutic Use (THU); Uses (USES) (anti-virulence C-mannoisdes as antibiotic-sparing, oral therapeutics for urinary tract infections)
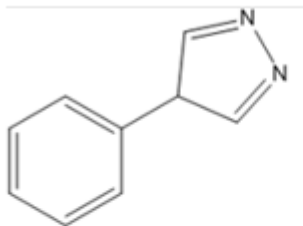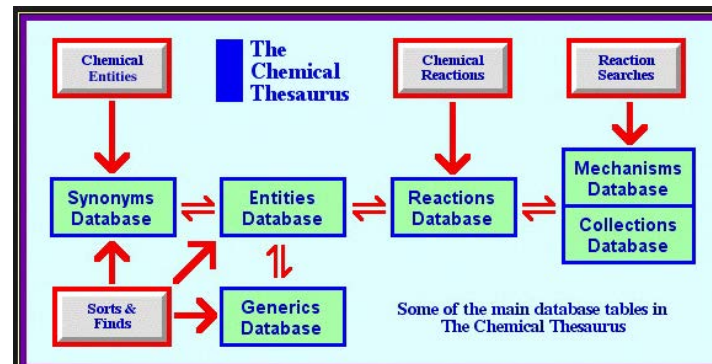
Future

- Give information professionals the tool to <u>merge</u> the results of compound searches from a variety of databases, proprietary, non-proprietary, open-source

- Structure-search value-add and full text databases sequentially or simultaneously and offer a similarity-ranked structure output
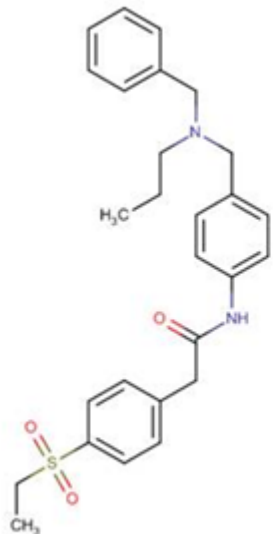
Mock Up:

CAS
DCR
REAXYS
PATBASE CHEMICAL EXPLORER

Future

HELP US DISPLAY OPEN-SOURCE DATA

- Example PUBCHEM

- Reaxys offers "deduping" of PubChem records against Reaxys retrieval

  - BUT some PUBCHEM Records offer unique references to substances

WO2015131035 (and associated patent family members); see pg. 98 where the compound in question is described as a "certain embodiment" of the invention and a previously published journal article is cited. The patent reference was indexed in **PubChem**.
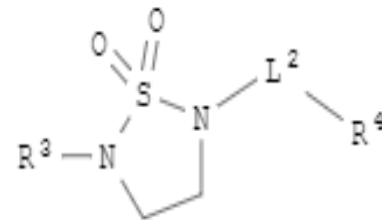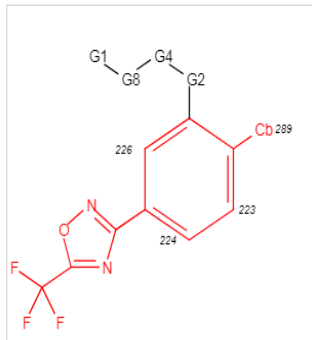
Future

- **Export of Markush structures as a table with related references**

    - Marpat/DWPIM

    - Export the hit Markush structure and reference

        - Minimize post-processing and maximize readability and information content in the Markush

        - Use colours to show structure overlap

        - New STN has made a good start, but the exportable "hit" Markush not always reflective of the true claim

Structure 1, Diagram 1 (Claim 1) Hide hit structure

Assembled

This is the actual claim structure!

Future

- **Text-mining** name-to-structure tools output

  - Databases offering text-mining name-to-structure tools

    - PatentScope

      - Currently NO structure-lead output

    - PatBase Chemical Explorer

      - Offers a structure-led output, but restricted use

    - Orbit

- **Text mine value-add, proprietary, open-source and full text databases sequentially or simultaneously and offer a similarity-ranked structure output**

- **Problem will be date and time stamps**

-**One last thought..**
-**Exemplified Prophetics in CAS:**

Patent number	Company	pages	records	Pr. compd
WO2015030217	Sumitomo Chem	277	329	2,247,630
US20080004323	Sumitomo Chem	177	123	778,674
WO2014004064	DuPont	205	108	737,072
US 2014005231	DuPont	104	108	737,072
WO2015016335	Sumitomo Chem	420	103	693,854

-**BizInt tables have no limits**
-**Word would crash!**
-**Do our attorneys need to see them all?**