

STN[®]

STN[®]: Searching for Patent Prior Art
Evidence of Obviousness

What evidence is required to evaluate the obviousness of a claimed invention?

- US Supreme Court decision in *KSR Int'l. Co v. Teleflex Inc.*, 550 U. S. _____, (2007)
 - Would it have been obvious to connect an adjustable vehicle control pedal to an electronic throttle control if both elements were shown to be in the prior art?
 - Is an **explicit suggestion** in the prior art to combine known elements also required to establish the obviousness of a combination invention?

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Session Agenda

- What types of prior art can be used to evaluate the obviousness of an invention?
- How is a legal determination of obviousness made in the US?
- STN[®] search strategies, tools, and resources to comprehensively identify prior art that indicates whether the invention in a patent claim would have been obvious

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When is a search for prior art evidence of obviousness conducted?

- Before an inventor files a patent application, to determine if the invention was obvious
- To determine the value of a granted patent or published patent application before acquiring patent rights or taking a license
- To invalidate existing patents during an infringement defense by showing that the claimed invention was obvious
- To assess the patentability of a patent application during examination at a patent office

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What is prior art?

- Everything publicly known
- Any disclosure or document that describes the invention in a patent claim in whole or in part, before a particular date
- Defined by national patent laws
 - In the US: Title 35, United States Code, Section 102

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What does the “prior” in prior art mean?

To constitute *prior art*, a reference must have a date:

- Before the effective filing date of the patent document being assessed (in Europe and other first-to-file patent systems). Effective filing date is determined by
 - Date of the filing of the earliest parent application
 - Date of filing of earliest foreign priority application
- OR
- Before the invention was made in the US and other first-to-invent patent systems
 - Can be shown by laboratory notebook evidence
 - The effective filing date of the patent document being assessed may be used as a starting point for comparison

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Possible dates for prior art references

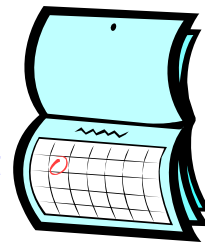
- Book, journal article
 - Publication date
 - Date available to public
- Patent document used as a prior art reference
 - Patent Grant date
 - Application publication date
 - Actual application filing date
 - Parent application filing date
 - Provisional filing date
- Historical prior art

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References that are prior art under 35 U.S.C. 102 can be used to establish obviousness

- 102(a): US patent applications and granted US patents **published before** the date of invention
- 102(b): Prior art in existence **more than one year before** the date of invention
- 102(e): US patents and published US and PCT applications **filed before** the date of invention by someone other than the inventors



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Date Indexes in CPlus

- **Application Date** /AD => S AD>20060900
- Application Date, Basic /AD.B => S 20050331/AD.B
- Application Year /AY => S 2004-2005/AY
- Application Year, Basic /AY.B => S AY.B>2006
- Cited Reference Publication Year /RPY => S 2003/RPY
- **Priority Application Date** /PRD => S PRD>20051211
- Priority Application Date, Basic /PRD.B => S PRD.B>20050630
- **Publication Date** /PD => S PD>20070106
- Publication Date, Basic /PD.B => S 20060923/PD.B
- Publication Year /PY => S 2007/PY
- Publication Year, Basic /PY.B => S 2006-2007/PY.B

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Date Indexes in USPATFULL

- **Application Date** /AD => S AD>20050900
- Application Year /AY => S 2005-2006/AY
- **Priority Date** /PRD => S 20031211/PRD
- Priority Year /PRY => S PRY>=2002
- **Publication Date** /PD => S 20040923/PD
- Publication Year /PY => S PY>=2005
- Reference Patent Publication Date /RPD => S DEC 2002/RPD
- Reference Patent Publication Year /RPY => S 2004/RPY
- **Related Application Date** /RLD => S 12 AUG 2004/RLD
- Related Application Year /RLY => S RLY<2005
- Related Patent Publication Year /RLPY => S 2007/RLPY

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A comprehensive prior art search looks for more than patent publications

Search for:

- Journals distributed before their cover date
- Dissertations catalogued in a university library
- Internet publications
- School textbooks
- Handouts or posters at a technical conference

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A comprehensive prior art search also looks for more than journal articles

Search for:

- Transcripts of lectures and discussions
- Publicly available products and devices
- Clinical trial information
- Pictures and drawings from design patents
- Fiction that describes the invention in sufficient detail

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Session Agenda

- What is Prior Art?
- How is a legal determination of obviousness made in the US?
- STN search strategies, tools and resources to comprehensively identify prior art that indicates whether the invention in a patent claim would have been obvious

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When is a claimed pharmaceutical obvious over related substances?

- *Eli Lilly v Zenith Goldline Pharmaceuticals*, 471 F.3d 1369 (Fed. Cir. 2006)
- Is a claim to olanzapine obvious over prior art teaching flumezapine, ethyl flumezapine or ethyl olanzapine?
 - Olanzapine differs from flumezapine by substitution of a H atom for the Cl atom at position 7 on the benzene ring
 - Olanzapine further differs from ethyl flumezapine by substitution of a methyl group for the ethyl group
 - Olanzapine differs from ethyl olanzapine by substitution of a methyl group for the ethyl group at the 3 position on the thiophene ring

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Statute 35 U.S.C. 103 (a) prohibits patenting of an obvious invention

A patent may not be obtained *though the invention is not identically disclosed or described as set forth in section 102 of this title*, if:

- The differences between the subject matter sought to be patented and the prior art are such that
 - The subject matter as a whole would have been obvious at the time the invention was made
 - To a person having ordinary skill in the art to which said subject matter pertains
- Patentability shall not be negated by the manner in which the invention was made

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Reference that establishes the lack of **novelty** of a claimed invention

- 35 U.S.C. 102
 - A patent claim is anticipated by a reference if the reference *teaches every aspect* of the claimed invention either explicitly or impliedly
 - Any feature of the claimed invention not directly taught by the reference must be inherently present

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References that establish the **obviousness** of a claimed invention

- 35 U.S.C. 103(a)
 - The primary reference does not teach every aspect of the claimed invention either explicitly or impliedly
 - The primary reference teachings must somehow be modified in order to meet the claims, for example, by combination with one or more other references
 - The modification must have been obvious to one of ordinary skill in the technology at the time the invention was made

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What is an obviousness search?

Obviousness searching involves a comparison of:

- The claimed invention in
 - A. a patent application whose patentability is being assessed or
 - B. a granted patent whose validity is being assessed
- Versus references which describe elements of the claimed invention

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Searching for prior art references to evaluate obviousness of a claimed invention

- Some inventions are combinations of elements
- Divide a combination invention into its parts (A+B+C+D+E)
- A, B, C, D and E may be
 - Components of a claimed mixture
 - Parts of a claimed device
 - Steps in a claimed method



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How does a novelty search differ from an obviousness search?

- A **novelty search** is a search for a single prior art reference teaching all parts of the invention (A+B+C+D+E) in the same reference
- An **obviousness search** is a search for multiple prior art references that teach less than all parts of the invention, e.g., (A+B+C+D) and (E), or (A+C+D) and (B+E), references that may be combined to teach the invention as a whole

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Novelty Search v. Obviousness Search

Claim 1. A diagnostic immunoassay kit comprising anti-HIV antibodies, phosphatase label, a buffer and a preservative.

- **Novelty Search**

- Search for a **single** reference teaching a diagnostic composition comprising the antibodies, phosphatase label, buffer and a preservative.

- **Obviousness Search**

- Search for **multiple** references that, combined together, teach a diagnostic composition comprising the antibodies, phosphatase label, a buffer and a preservative.

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Searching for prior art evidence of the obviousness of a combination invention

Search Question:

What prior art earlier than 2006 describes a diagnostic immunoassay kit for detecting HIV viral antigens in a body fluid sample, the kit containing anti-HIV antibodies coupled to a peroxidase label, a buffer and a preservative?

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Overall Search Strategy

1. Identify files to search
2. Use online thesauri to develop a search query in one file
3. Refine answer sets by date
4. Identify single references that teach all the claimed components
5. Identify references that can be combined to teach the claimed components
6. Optional: Extend search to other files

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Use the INDEX command to screen files for the technology of interest

```
=> INDEX BIOSCIENCE CHEMISTRY MEDICINE
INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
DRUGMONOG, DRUGMONOG2, DRUGU, ...'
93 FILES IN THE FILE LIST IN STNINDEX

=> S KIT AND ANTIBOD? AND ENZYM?
L1 QUE KIT AND ANTIBOD? AND ENZYM?

=> D RANK
F1      82854   DGENE
F2      77774   USPATFULL
F3      9400    USPAT2
F4      6047    WPIDS
F5      6047    WPINDEX
F6      5361    CAPLUS
F7      4334    IFIPAT
F8      3840    BIOTECHABS
F9      3840    BIOTECHDS
F10     2742    MEDLINE
```

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Use the CA Lexicon to explore synonyms for the 'antibodies' concept

=> FILE ZCAPLUS

=> E ANTIBODIES/CT

E#	FILE	FREQUENCY	AT	TERM
E1	ZCAPLUS	0	1	ANTIBLOCKING/CT
E2	ZCAPLUS	749	4	ANTIBLOCKING AGENTS/CT
E3	ZCAPLUS	132837	2 -->	ANTIBODIES/CT
E4	ZCAPLUS	0	2	ANTIBODIES (L) ALLO-/CT
E5	ZCAPLUS	0	2	ANTIBODIES (L) ALLOANTIBODIES/CT

Explore synonyms for "antibodies" in the zero-connect hour ZCAPLUS file.

=> E E3+ALL

E#	FILE	FREQUENCY	TERM
E13	ZCAPLUS	132837	--> Antibodies/CT HNTE Valid heading during volumes 86-135 (1977-2001) only.
E14	ZCAPLUS	99222	NEW Antibodies and Immunoglobulins/CT

***** END *****

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Use the CA Lexicon to explore synonyms (cont)

=> E E14+ALL

E#	FILE	FREQUENCY	TERM
E15	ZCAPLUS	11912	BT4 Chemical compounds/CT
E16	ZCAPLUS	11358	BT3 Macromolecular compounds/CT
E17	ZCAPLUS	11912	BT4 Chemical compounds/CT
E18	ZCAPLUS	46718	BT3 Organic compounds/CT
E19	ZCAPLUS	898524	BT2 Proteins/CT
E20	ZCAPLUS	38540	BT1 Globulins/CT
E21	ZCAPLUS	0	BT1 Immune factors (non-CA heading)/CT
E22	ZCAPLUS	99222	--> Antibodies and Immunoglobulins/CT HNTE Valid heading during volume 136 (2002) to present.
E23	ZCAPLUS	1	OLD Allergins/CT
E24	ZCAPLUS	6	OLD Anamnestic reaction/CT
E25	ZCAPLUS	132837	OLD Antibodies/CT
E26	ZCAPLUS	2	OLD Antibody/CT
E27	ZCAPLUS	9206	OLD Globulins, immune/CT
E28	ZCAPLUS	66872	OLD Immunoglobulins/CT
•••			
E68	ZCAPLUS	1518	RT V(D)J recombination/CT

***** END *****

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Search Lexicon terms in HCAplus

```

=> FILE HCAPLUS
=> S E22-E49
L2 298369 ("ANTIBODIES AND IMMUNOGLOBULINS"/CT OR
      TIC REACTION"/CT OR ANTIBODIES/CT OR
      IMMUNE"/CT OR IMMUNOGLOBULINS/CT OR "G
      I"/CT OR IG/CT OR "IMMUNE BODIES"/CT OR
      IMMUNOGLOBULIN/CT OR POLYGAM/CT OR "POL
      ULIN/CT OR TEGELINE/CT OR "VIAGAM S"/CT
      CT OR ANTITOXINS/CT OR ANTIVENOMS/CT OR
      N/CT OR INFILXIMAB/CT OR "MUROMONAB CD
      S"/CT OR RITUXIMAB/CT)
  
```

Search the synonyms for "antibodies" in the HCAplus file for search term cost savings. These heavily posted generic terms are searching in the index term fields to maximize search precision but terms may also be searched in the basic index to maximize retrieval.

```

=> FILE ZCAPLUS
  
```

```

=> E PRESERVATIVE/CT
  
```

E#	FILE	FREQUENCY	AT	TERM
E69	ZCAPLUS	0	7	PRESERVATION SOLUTIONS (TISSUE) (L) M-K YOTO/CT
E70	ZCAPLUS	0	10	PRESERVATION SOLUTIONS (TISSUE) (L) UNIVERSITY OF WISCONSIN SOLUTION/CT
E71	ZCAPLUS	0	1	--> PRESERVATIVE/CT
E72	ZCAPLUS	7315	17	PRESERVATIVES/CT

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...
  
```

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Explore synonyms in the CA Lexicon

```

=> E E72+ALL
  
```

E#	FILE	FREQUENCY	TERM
E301	ZCAPLUS	18337	BT1 Materials/CT
E302	ZCAPLUS	7315	--> Preservatives/CT HNTD Valid heading during volume 1 (1907) to present.
E303	ZCAPLUS	80913	NT1 Antioxidants/CT
E304	ZCAPLUS	1142	NT2 Antiozonants/CT
E305	ZCAPLUS	0	NT2 DL-Selenomethionine/CT
E306	ZCAPLUS	0	NT2 Dodecyl gallate/CT
...			
E314	ZCAPLUS	38519	RT Fungicides/CT
E315	ZCAPLUS	3005	RT Preservation/CT
E316	ZCAPLUS	12658	RT Stabilizing agents/CT
E317	ZCAPLUS		RTCS Chlorobutanol/CT

Search the synonyms for the 'preservatives' concept.

```

***** END *****
  
```

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Create sets for each component

```

=> FILE HCAPLUS
=> S E302-303, E308-311, E314-316
L3 161159 (PRESERVATIVES/CT OR ANTIOXIDANTS/CT OR "HEAVY METALS"
OR "LIGHT STABILIZERS"/CT OR "UV STABILIZERS"
OR "SOLUBLE FILMS" OR "SOLUBLE FILM SOLUTIONS (TISSUE)"/CT OR FUNGICIDES/CT OR
"STABILIZING AGENTS"/CT)
=> FILE ZCAPLUS
=> E BUFFERS/CT
E# FILE FREQUENCY AT TERM
---
E1 ZCAPLUS 1 BUFFERING POWER/CT
E2 ZCAPLUS 0 2 BUFFERING SUBSTANCES/CT
E3 ZCAPLUS 9655 14 --> BUFFERS/CT
E4 ZCAPLUS 0 2 BUFFING/CT

=> E E3+ALL
E# FILE FREQUENCY TERM
---
E13 ZCAPLUS 9655 --> Buffers/CT
HNTD Valid heading during volume 66 (1967)
to present.
E14 ZCAPLUS 2 OLD Buffer/CT
E15 ZCAPLUS 316 OLD Buffer substances/CT
E16 ZCAPLUS 162 OLD Buffer substances and Buffer systems/CT
E17 ZCAPLUS 3638 OLD Buffer substances and systems/CT
E18 ZCAPLUS 589 OLD Buffer systems/CT
E19 ZCAPLUS UF Buffering agents/CT
E20 ZCAPLUS UF Buffering substances/CT
E21 ZCAPLUS UF Std. buffer substances/CT
    
```

Search the synonyms for the 'preservatives' concept.

Explore the synonyms for the 'buffers' concept.

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Create sets for each component

```

=> FILE HCAPLUS
=> S E13-E20
L4 14360 (BUFFERS/CT OR BUFFER/CT OR "BUFFER SUBSTANCES"/CT OR "BUFFER
SUBSTANCES AND BUFFER SYSTEMS"/CT OR "BUFFER
SYSTEMS"/CT OR "BUFFER SYSTEMS"/CT OR "BUFFERING
SUBSTANCES"/CT)
=> FILE ZCAPLUS
=> E PEROXIDASE/CT
E# FILE FREQUENCY AT TERM
---
E1 ZCAPLUS 0 1 PEROWSKIANUM/CT
E2 ZCAPLUS 0 1 PEROX/CT
E3 ZCAPLUS 0 21 --> PEROXIDASE/CT

=> E E3+ALL
E# FILE FREQUENCY TERM
---
E13 ZCAPLUS 11912 BT5 Chemical compounds/CT
E14 ZCAPLUS 11358 BT4 Macromolecular compounds/CT
E15 ZCAPLUS 11912 BT5 Chemical compounds/CT
E16 ZCAPLUS 46718 BT4 Organic compounds/CT
E17 ZCAPLUS 898524 BT3 Proteins/CT
E18 ZCAPLUS 192447 BT2 Enzymes/CT
E19 ZCAPLUS 0 BT1 Oxidoreductase/CT
E20 ZCAPLUS 0 --> Peroxidase/CT
E21 ZCAPLUS 1 OLD Peroxidases/CT
E22 ZCAPLUS UF E.C. 1.11.1.7/CT
    
```

Search the synonyms for the 'buffers' concept.

Explore the synonyms for the peroxidase label.

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Create sets for each component

```

=> FILE HCAPLUS

=> S E20-22
    43284 PEROXIDASE/CT (1 TERM)
      1 PEROXIDASES/CT
      0 "E.C. 1.11.1.7"/CT
L5    43285 (PEROXIDASE/CT OR PEROXIDASES/CT OR "E.C. 1.11.1.7"/CT)

=> FILE ZCAPLUS
=> E HIV/CT
E#   FILE           FREQUENCY   AT   TERM
--   ----           -
E1   ZCAPLUS        0         1   HIULCA/CT
E2   ZCAPLUS        0         1   HIURAI/CT
E3   ZCAPLUS        0         3   --> HIV/CT
E4   ZCAPLUS        0         2   HIV (DISEASE)/CT
E5   ZCAPLUS        0         2   HIV COMBINATION CHEMOTHERAPY/CT
E6   ZCAPLUS        0         2   HIV I/CT
E7   ZCAPLUS        0         2   HIV II/CT
    
```

Search the synonyms for the peroxidase label.

Explore the synonyms for HIV.

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Create sets for each component

```

=> E E3+ALL
E#   FILE           FREQUENCY   TERM
--   ----           -
E13  ZCAPLUS        0         --> HIV/CT
E14  ZCAPLUS        7545      USE Human immunodeficiency virus/CT
E15  ZCAPLUS        31924     USE Human immunodeficiency virus 1/CT
***** END *****

=> E E6+ALL
E#   FILE           FREQUENCY   TERM
--   ----           -
E16  ZCAPLUS        0         --> HIV I/CT
E17  ZCAPLUS        31924     USE Human immunodeficiency virus 1/CT
***** END *****

=> FILE HCAPLUS
=> S E14-E15
    7545 "HUMAN IMMUNODEFICIENCY VIRUS"/CT
    31924 "HUMAN IMMUNODEFICIENCY VIRUS 1"/CT
L6    38347 ("HUMAN IMMUNODEFICIENCY VIRUS"/CT OR "HUMAN IMMUNODEFICIENCY
      VIRUS 1"/CT)
    
```

Explore and search the synonyms for HIV.

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Novelty search has all 5 components

```

=> S L2 AND L3 AND L4 AND L5 AND L6
L7      1 L8 AND L9
=> D L7 1 BIB
L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS
AN 2001:397169 HCAPLUS
DN 135:2526
TI Devices and methods for detecting analytes
capture reagent
IN Zhang, Honghua
PA Biotronic Technologies, Inc., USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO.          KIND    DATE          APPLICATION NO.    DATE
-----
PI WO 2001038873     A2    20010531     WO 2000-US29748   20001027
  WO 2001038873     A3    20020711
  W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, ...
US 6670115          B1    20031230     US 2000-699140    20001027
  TW 224673          B     20041201     TW 2000-89125029  20001124
  US 2004096991     A1    20040520     US 2003-704470    20031107
PRAI US 1999-167409P P     19991124
  US 2000-699140     A     20001027
  
```

The **novelty** search for a single reference that teaches all 5 components of the kit finds one reference.

Concepts:

L2=antibodies

L3=preservative

L4=buffer

L5=peroxidase label

L6=HIV

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HIT display shows terms searched

```

=> D L7 1 HIT
L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
IT Buffers
  Fluids
  Liquids
  (anal. of; devices and methods for detecting analytes using
  electrosensor having capture reagent)
IT Hepatitis A virus
  Hepatitis B virus
  Hepatitis C virus
  Human immunodeficiency virus
  (analyte as marker for infection with; devices and methods for
  detecting analytes using electrosensor having capture reagent)
IT Amino acids, uses
  Antibodies
...
  Stabilizing agents
  Test kits
...
IT 9003-99-0D, Peroxidase, conjugates with .alpha.-fetoprotein or
with antibody or immobilized
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(devices and methods for detecting analytes using electrosensor having
capture reagent)
IT 9003-99-0, Peroxidase
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(horseradish, as label; devices and methods for detecting analytes
using electrosensor having capture reagent)
  
```

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Obviousness search combines prior art

```

=> S (L2 AND L3 AND L4 AND L5) AND (PY<2006 OR AY<2006)
L8 15 (L2 AND L3 AND L4 AND L5) AND (PY<2006 OR AY<2006)
=> D 2 BIB ABS HIT
L8 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:871134 HCAPLUS
DN 145:247525
TI Equine herpes virus-1 antigen coated on solid support for
antibody and diagnosing equine herpes virus-1 disease
IN Rattan, Bharatander; Singh, Birender Kumar; Yadav, Mahesh
Asmok Kumar
PA Indian Council of Agricultural Research, India
SO Indian, 22 pp. CODEN: INXXAP
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO.
-----
PI IN 191278 A1 20031025 IN 1996-DE2199
PRAI IN 1996-DE2199 19961009
AB A method for the prepn. of a diagnostic kit useful for
antibodies against equine herpes virus 1 causing abortus
disorder in equines, the method comprising the steps of
obtaining equine herpes viral antigen ext. in a manner
described, b) coating a solid surface such as herein de
antigen ext. of step (a), c) blocking uncoated sites of
with a blocking agent such as herein described, d) stabilizing the coated
antigen on the solid surface in a known manner such as to prep. it in a
ready-to-use state, e) providing sera from equines free of equine herpes
virus to serve as neg. control sera, f) providing sera from equines
immunized with herpes virus 1 to serve as pos. control, g) providing
anti-species antibodies and conjugating it with an enzyme to obtain
antispecies globulin-enzyme conjugate, and h) providing an enzyme
substrate soln. such as herein described to obtain a kit.
    
```

The **obviousness** search looks for prior art references that teach some but not all of the concepts of the invention and that may be combined to teach the invention as a whole. This search identifies 15 primary references that teach the:

- L2=antibodies
- L3=preservative
- L4=buffer
- L5=peroxidase concepts.

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Only 4 sets of concepts are included

```

Buffers
Centrifugation
Color formers
Equus caballus
Microtiter plates
Stabilizing agents
Test kits
(equine herpes virus-1 antigen coated on solid support for
antibody and diagnosing equine herpes virus-1 disease)
IT Antibodies and Immunoglobulins
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(equine herpes virus-1 antigen coated on solid support for detecting antibody and diagnosing equine herpes virus-1 disease)
IT Antibodies and Immunoglobulins
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(labeled; equine herpes virus-1 antigen coated on solid support for detecting antibody and diagnosing equine herpes virus-1 disease)
IT 7722-84-1, Hydrogen peroxide, biological studies 9001-78-9, Alkaline phosphatase 9003-99-0, Peroxidase 9005-64-5, Tween 20
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(equine herpes virus-1 antigen coated on solid support for detecting antibody and diagnosing equine herpes virus-1 disease)
    
```

The Index Term fields show the controlled terminology searched for four of the five concepts in the claim, but does not describe the use of peroxidase-labeled anti-HIV antibodies.

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Try alternative combinations of sets

```

=> S L2 AND L5 AND L6 AND (PY<2006 OR AY<2006)
L9 73 L3 AND L7 AND L9 AND (PY<2006 OR AY<2006)

=> D L9 1 BIB ABS
L9 ANSWER 1 OF 73 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1252337 HCAPLUS
DN 146:26352
TI HIV-1 p24 antigen, antibody and ELISA test kit for di
infection and detecting HIV-1 contamination of blood
preparations
IN Moriyama, Masami; Tanaka, Yuetsu
PA Japan
SO PCT Int. Appl., 22pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126287	A1	20061130	WO 2005-JP15857	20050831 <--
JP 2005-155326	A	20050527		

AB A method for detecting HIV-1 reliably that can be used for the diagnosis of HIV-1 infection simply and reliably and a kit to be used for the method are provided. The method for detecting HIV-1 in human serum, a human serum-derived blood prepn. or serum for transfusion by an ELISA method characterized by using an antibody (anti-HIV-1 p24 antibody) that recognizes and binds to p24 antigen (HIV-1 p24) that is expressed in human immunodeficiency virus (HIV-1) in the growth phase, the method for detecting human-derived p24 antibody in the serum and an ELISA kit for detecting HIV-1 p24 antigen/antibody to be used for the method are provided.

This search identifies 73 prior art references which teach the antibodies (L2), peroxidase (L5), and HIV (L6) concepts. Some of these references may be combined with the references from the previous answer set as evidence of obviousness of the claimed kit.

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Other types of prior art references that could be combined

- A reference showing a core structure and a substituent and a reference suggesting that a different substituent would provide an advantage
- A reference showing close homologues and teaching that the homologues share properties with a claimed substance
- A reference showing a biosequence and a reference suggesting conservative substitutions to that sequence would function identically

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Prior art references may come from the inventor's or analogous technologies

- Analogous prior art
 - References in the field of applicant's endeavor
 - References reasonably pertinent to the particular problem with which the inventor was concerned
- References must enable others to make and use the claimed invention

STN

39

The Supreme Court established the analysis for obviousness of a claimed invention

1. Determine the scope and contents of the prior art
2. Ascertain the differences between the prior art and the claims in issue
3. Resolve the level of ordinary skill in the pertinent art
4. Evaluate evidence of secondary considerations

Graham v. John Deere, 383 U.S. 1, 148 USPQ 459 (1966)

STN

40

Criteria for establishing the obviousness of a claimed invention

1. The prior art references when combined must teach or suggest all the claim limitations
2. An apparent reason to combine the prior art references may be found in
 - The prior art references
 - The nature of the problem
 - The knowledge of a person having ordinary skill and creativity in the technology
 - Secondary considerations must also be evaluated

STN

41

It would have been obvious to combine the references...

- In the absence of unexpected results
 - To omit unnecessary elements
 - To automate a manual process
 - To substitute recognized equivalents for the same purpose
 - To optimize a process through routine experimentation

STN

42

Reasonable expectation of success
is required to show obviousness
of a claimed invention

- Prior art can be combined to reject claims as obvious as long as there is a reasonable expectation of success
- Obviousness does not require absolute predictability, however, at least some degree of predictability is required
- Evidence showing there was *no* reasonable expectation of success may support a conclusion of non-obviousness (reference teaches away)

STN

43

If there is a reasonable expectation
of success ...

- *KSR Int'l. Co v. Teleflex Inc.*, 550 U. S. _____, (2007), No. 04-1350 (April 30, 2007)
- It would have been obvious to connect an adjustable vehicle control pedal to an electronic throttle control because
 - Both elements were known in the prior art
 - The combination “does no more than yield predictable results”

STN

44

But if the *prior art teaches away from the invention...*

- *Eli Lilly v. Zenith Goldline Pharmaceuticals* 471 F.3d 1369 (Fed. Cir. 2006)
- A claim to olanzapine is *not* obvious over prior art teaching flumezapine, ethyl flumezapine or ethyl olazapine because...
- One of ordinary skill in the art would have expected that replacing the fluorine atom with a hydrogen atom would produce a compound *without sufficient antipsychotic activity*
- If one were looking to replace the fluorine, one would replace the fluorine with other electronegative groups, not hydrogen. Indeed, the art as a whole teaches directly away from using hydrogen because it is not an electron-withdrawing substituent

STN

45

Evaluating secondary considerations as indicia of nonobviousness

- Long felt but unresolved needs
- Failure of others to make the invention
- Commercial success of the invention

STN

46

Secondary considerations may establish non-obviousness

- Zyprexa Patent Upheld on Appeal
 - “The record shows a long-felt need for a safer, less toxic, and more effective clozapine-like drug; a decade (or more) of failure to find a replacement for clozapine; a reasonable amount of commercial success for olanzapine; and a number of awards for olanzapine as indicators of industry acclaim.”
Eli Lilly v. Zenith Goldline (Fed. Cir. 2006)

STN

47

Search for 3 types of information for a comprehensive obviousness search

1. Search for prior art references that, when combined, teach all the limitations of the patent claim
2. Search for information that suggests a reason to combine the references or for references that “teach away” from the invention
3. Search for information that addresses secondary considerations

STN

48

How many references can be used to show obviousness of a claimed invention?

- Reliance on a large number of references does not, without more, weigh against the obviousness of the claimed invention
 - Federal Circuit Court affirmed a rejection of a detailed claim to a candy sucker shaped like a thumb on a stick based on **thirteen** prior art references

***Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991)**

STN

49

Session Agenda

- What is Prior Art?
- How is a legal determination of obviousness made?
- STN search strategies, tools and resources to comprehensively identify prior art that indicates whether the invention in a patent claim would have been legally obvious

STN

50

Searching for references that show obviousness of a chemical substance

- Search for
 - Structural homologues
 - Salts
 - Mixtures
 - Isomers
 - Derivatives
 - Radio-labeled molecules
 - Fragments
 - Fused molecules

STN

51

Searching for references that show obviousness of a chemical substance

- Substructure search in CAS REGISTRYSM and MARPAT[®]
- Maximize variability
 - STN-defined variables
 - Unspecified bonds
 - Repeating groups
 - G-groups
 - Ring/Chain nodes and bonds (REGISTRY only)
- Chart the results for an overview of the prior art
 - STN Express[®] R-Group Analysis chart
 - STN Express RN and Role Report

STN

52

Searching for prior art evidence of the obviousness of a chemical substance

Search Question:

What prior art earlier than 1995 describes the therapeutic use of variants, derivatives or mixtures containing the bisulfate salt of the d-enantiomer of methyl alpha-5-(4,5,6,7-tetrahydro(3,2-c)thienopyridyl)-(2-chlorophenyl) acetate, (clopidogrel bisulfate), the active ingredient in Plavix®?

STN

53

Overall Search Strategy

1. Locate the substance record in REGISTRY
2. Create a structure query and conduct a substructure search in REGISTRY
3. Create a R-group table from the answer set
4. Cross over to CAplusSM and search using CAS Roles and date refinements
5. Extend the search to MARPAT
6. Remove duplicates and display results

STN

54

Verify and search the chemical name in the REGISTRY file

```

=> FILE REGISTRY

=> E PLAVIX/CN
E#      FILE                FREQUENCY  TERM
--      ---                -
E1      REGISTRY            1          PLAVEST ST 20/CN
E2      REGISTRY            1          PLAVEST ST 700/CN
E3      REGISTRY            1 -->      PLAVIX/CN
E4      REGISTRY            1          PLAVOLEX/CN
E5      REGISTRY            1          PLAWET G 140H/CN
E6      REGISTRY            1          PLAX/CN
E7      REGISTRY            1          PLAX 885/CN
E8      REGISTRY            1          PLAXENE 185/CN
E9      REGISTRY            1          PLAXENE 190/CN
E10     REGISTRY            1          PLAXENE 6110/CN
E11     REGISTRY            1          PLAXICEL/CN
E12     REGISTRY            1          PLAXYLOSIDE/CN

=> S E3
L1      1 PLAVIX/CN

=> D
  
```

STN

55

Substance identification information

```

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 120202-66-6 REGISTRY
ED Entered STN: 21 Apr 1989
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, (aS)-, sulfate (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, (S)-, sulfate (1:1)
OTHER NAMES:
CN (S)-(+)-Methyl (2-chlorophenyl)(6,7-dihydro-4H-thieno[3,2-c]pyrid-5-yl)acetate
bisulfate
CN (S)-(+)-Methyl 2-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-
yl)acetate hydrogen sulfate
CN Clopidogrel bisulfate
CN Clopidogrel hemisulfate
CN Clopidogrel hydrogen sulfate
CN Iscover
CN Methyl (S)-(4,5,6,7-tetrahydrothieno[3,2-c]pyridin-5-yl)(2-
chlorophenyl)ethanoate hydrogen sulfate
CN Plavix
CN SR 25990C
FS STEREOSEARCH
MF C16 H16 Cl N O2 S . H2 O4 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB*,
IMSCOESEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE,
PATDPASPC, PROMT, PROUSDDR, PS, SCISEARCH, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)
  
```

STN

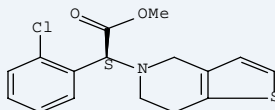
56

Structure information

CM 1

CRN 113665-84-2
CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
CMF H2 O4 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

164 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
164 REFERENCES IN FILE CAPLUS (1907 TO DATE)

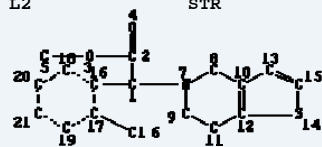
STN

57

Model on a CAS RN using the STRUCTURE (STR) command

```
=> STR 113665-84-2
:END
L2 STRUCTURE CREATED
```

```
=> D L2
L2 HAS NO ANSWERS
L2 STR
```



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

STN

Consider searching the flat structure for clopidogrel bisulfate, omitting the sulfate, using unspecified bonds, and/or substituting halogen for chlorine. For pharmaceuticals, drawing a query structure having close structural similarity to the claimed structure is suggested to maintain a reasonable expectation of similar activity *in vivo* than for other chemicals.

58

Run structure search

```
=> S L2 SSS SAM
SAMPLE SEARCH INITIATED 16:29:42
SAMPLE SCREEN SEARCH COMPLETED -      12 TO ITERATE

100.0% PROCESSED      12 ITERATIONS      9 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:   33 TO    447
PROJECTED ANSWERS:      9 TO    360

L3          9 SEA SSS SAM L2

=> S L2 SSS FULL
FULL SEARCH INITIATED 14:47:59
FULL SCREEN SEARCH COMPLETED -
100.0% PROCESSED      170 ITERATIONS
141 ANSWERS
SEARCH TIME: 00.00.01
L4          141 SEA SSS FUL L2
```

Substructure searching will retrieve the query structure as well as stereoisomers, isotopically labeled molecules, salts, mixtures and the query structure substituted at open sites.

STN

59

Use D SCAN to evaluate substances

```
=> D SCAN

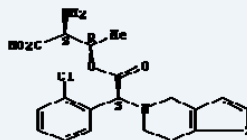
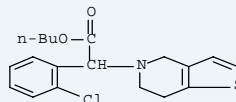
L4 141 ANSWERS  REGISTRY  COPYRIGHT 2007 ACS on STN
IN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-
dihydro-, butyl ester (9CI)
MF C19 H22 Cl N O2 S
CI COM

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 141 ANSWERS  REGISTRY  COPYRIGHT 2007 ACS on STN
IN Thieno[3,2-c]pyridine-5(4H)-acetic acid, (+)-(2-chlorophenyl)-6,7-
dihydro-, (1R,2S)-2-amino-2-carboxy-1-methylethyl ester, (+-S)- (9CI)
MF C19 H21 Cl N2 O4 S
CI COM

Absolute stereochemistry. Rotation (+).
```



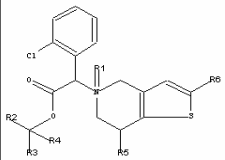
STN

60

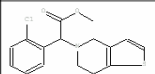


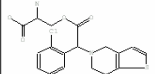
R-Group Analysis Table

STN Online and Results - [Table Output - plavix revised.tbl]

File Edit Preferences Web Window Help



A R-Group Analysis Table can be created to provide an overview of related prior art structures.

Answer	CAS Registry Number*	Index Name	R1	R2	R3	R4	R5	R6	Structure	Other Components
L6 1 OF 141 REGISTRY	917973-28-5 REGISTRY	Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, (α S)-, methyl ester, phosphate (1-7)	none	H	H	H	H	H		
L6 2 OF 141 REGISTRY	913473-88-8 REGISTRY	Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, (2S)-2-amino-2-carboxyethyl ester, (α S)- (9CI)	none		H	H	H	H		

Edit transcript

Look for therapeutic uses in CAPLUS

```

=> FILE CAPLUS
=> S L4/THU
      1269 L4
      887376 THU/RL
L5    1115 L4/THU
      (L4 (L) THU/RL)
  
```

Use the THU CAS Role in CAPLUS to refine the answer set to records in which the clopidogrel bisulfate - related substances have therapeutic activity.

```

=> D L5 KWIC 1115
L5 ANSWER 1115 OF 1115 CAPLUS COPYRIGHT 2007 ACS on STN
IT 115608-70-3P 115608-71-4P 115608-72-5P
   115608-73-6P 115608-74-7P 115608-75-8P
   115608-76-9P 115608-77-0P 115608-78-1P
   115608-79-2P 115608-80-5P 115608-81-6P
   115608-82-7P 115608-83-8P 115608-84-9P
   115608-85-0P 115608-86-1P 115608-87-2P 115608-88-3P
   115608-89-4P 115608-90-7P 115653-25-3P
RL: BAC (Biological activity or effector, except adverse);
     BSU (Biological study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(prepn.
     of, as antithrombotic)
  
```

```

=> S L5 AND (PY<1995 OR AY<1995)
      16106608 PY
      2859614 AY<
L6    13 L5
  
```

Limit the answer set to references which are prior art based on their **publication** or **application dates** using year or date codes. Specific patent country codes (US, WO, etc.) can be linked to date search for more precision.

STN

62

Prior art based on application date

=> D L6 3 IBIB ABS HITSTR

L6 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:722513 HCAPLUS Full-text
 DOCUMENT NUMBER: 126:1200
 TITLE: Method for the secondary prevention of ischemic events
 INVENTOR(S): Herbert, Jean-marc; Frehel, Daniel; Bernat, Andre; Badorc, Alain; Savi, Pierre; Delebassee, Denis; Kieffer, Gilles; Defreyn, Ghislain; Maffrand, Jean-pierre
 PATENT ASSIGNEE(S): Elf Sanofi SA, Fr.
 SOURCE: U.S., 5 pp
 CODEN: US
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

Although this US patent was granted after the 1995 critical date, it is prior art based on its 1994 application filing date.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5576328	A	19961119	US 1994-190332	19940131 <--
PRIORITY APPLN. INFO.:			US 1994-190332	19940131

STN

63

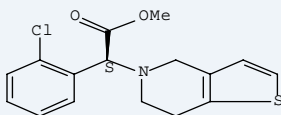
HITSTR display includes structure

AB The invention relates to a new method for the secondary prevention of ischemic events comprising administering to a man a therapeutically effective amount of a compound selected from clopidogrel and its pharmaceutically acceptable acid addition salts in association with a pharmaceutically acceptable carrier...

IT 113665-84-2, Clopidogrel 120202-66-6, Clopidogrel hydrogen sulfate
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (clopidogrel for secondary prevention of ischemic events)

RN 113665-84-2 HCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



The HITSTR display shows the RN, chemical name and structure that match the search query in the context of the publication record.

STN

64

RN & Role Report

Microsoft Excel - plavix rn and role report sorted.xls

File Edit View Insert Format Tools Data Window Help WebEx Adobe PDF

100% Magnification

Sort Column Delete Column Combine

S1 PEP (Physical, engineering or chemical process)

	A	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH
1		BAC (Biological activity or effector, accept address)	SPN (Synthetic preparation)	RACT (Reactant or reagent)	RCT (Reactant)	PRP (Properties)	DMA (Drug mechanism of action)	PROC (Process)	IMF (Industrial manufacture)	PKT (Pharmacokinetics)	PEP (Physical, engineering or chemical process)	ANST (Analytical study)	PYP (Physical process)	ANT (Analyte)	BPR (Biological process)	PUR (Purification or recovery)	PNU (Preparation, unclassified)	BLU (Biological use, unclassified)	FORM (Formation, nonseparatable)	CPS (Chemical process)	DEV (Device component use)	FMU (Formation, unclassified)	BCP (Biochemical process)	BYP (Byproduct)	MSC (Miscellaneous)	TEM (Technical or engineered material used)
2	113665-84-2	132	37	50	49	9	52	19	18	27	6	12	4	11	12	6	6	6	1	1	3	1	1		2	2
3	120202-66-6	10	43	11	11	29	2	10	15	7	9	7	8	7									1			
4	120202-69-9	2	4	6	6	1	1	3	2		1	2		2	1	1			1	1				2		
5	90055-48-4	1	16	12	12	1		2	4		1	2		2					1	1						
6	113665-84-2D	1	3	1	1	3		1	1		1		1				1	1								
7	115608-70-3	1	3	2	2				1																	
8	115608-71-4	1	1																							
9	115608-72-5	1	1																							
10	115608-73-6	1	1																							
11	115608-74-7	1	1																							
12	115608-75-8	1	1																							

Ready

Extend to MARPAT

```

=> FILE MARPAT
=> S L4 SSS SAM
SAMPLE SEARCH INITIATED 15:48:08
SAMPLE SCREEN SEARCH COMPLETED -
100.0% PROCESSED 32 ITERATI
SEARCH TIME: 00.00.01
FULL FILE PROJECTIONS: ONLINE *
                        BATCH *
PROJECTED ITERATIONS: 30
PROJECTED ANSWERS:
L7 3 SEA SSS SAM L4

=> S L4 SSS FULL
FULL SEARCH INITIATED 15:48:34
FULL SCREEN SEARCH COMPLETED - 700 TO ITERATE
100.0% PROCESSED 700 ITERATIONS 22 ANSWERS
SEARCH TIME: 00.00.03
L8 22 SEA SSS FUL L4

=> SET DUPORDER FILE
=> DUP REM L8 L6
L9 34 DUP REM L8 L6 (1 DUPLICATE REMOVED)
ANSWERS '1-22' FROM FILE MARPAT
ANSWERS '23-34' FROM FILE CAPLUS

=> D L9 22 IBIB QHIT
    
```

- Use the L-number from the REGISTRY file answer set (L4) to extend the search to the MARPAT file at a reduced cost
- 22 patents are identified with Markush claims that include the structure query

STN

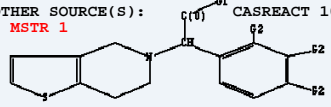
QHIT shows query-focused display

L9 ANSWER 22 OF 34 MARPAT COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 100:191856 MARPAT [Full-text](#)
 TITLE: Thieno[3,2-c]pyridine derivatives and their
 therapeutical use
 INVENTOR(S): Aubert, Daniel; Ferrand, Claude; Maffrand, Jean Pierre
 PATENT ASSIGNEE(S): Sanofi, Fr.
 SOURCE: Eur. Pat. Appl., 20 pp.CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 99802	A1	19840201	EP 1983-401382	19830705
EP 99802	B1	19870204		

...
 PRIORITY APPLN. INFO.: FR 1982-12599 19820713
 EP 198
 CS 198

OTHER SOURCE(S): CASREACT 100:191856
 MSTR 1



G1 = OMe
 G2 = Cl
 Patent location: claims
 Note: record may include structures from disclosure

The oldest MARPAT record shows the Cl and MeO substituents as G-groups.

STN

67

MARPAT patents with prior art dates earlier than 1995 can be identified in CAPLUS

```
=> FILE CAPLUS
=> S L8 AND (PY<1995 OR AY<1995)
      22 L8
      16092074 PY<1995
      2853659 AY<1995
L10   3 L8 AND (PY<1995 OR AY<1995)
=> D 110 1 IBIB ABS
```

STN

68

Several members of this patent family are prior art based on publication dates

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:194139 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 116:194139
 TITLE: Isopropyl 2-thienylglycidate, process for its preparation, and its use as synthetic intermediate for ticlopidine and clopidogrel
 INVENTOR(S): Bousquet, Andre; Calet, Serge; Heymes, Alain
 PATENT ASSIGNEE(S): Sanofi SA, Fr.
 SOURCE: Eur. Pat. Appl., 11 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 465358	A1	19920108	EP 1991-401833	19910703 <--
EP 465358	B1	19960207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2664276	A1	19920110	FR 1990-8482	19900704 <--
...				
AT 133950	T	19960215	AT 1991-401833	19910703 <--
ES 2083542	T3	19960416	ES 1991-401833	19910703 <--
PRIORITY APPLN. INFO.:			FR 1990-8482	A 19900704
OTHER SOURCE(S):			CASREACT 116:194139; MARPAT 116:194139	

STN

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Abstract graphic shows key structure



This structure was published in the source patent document.

AB Title ester I, useful as an intermediate for antithrombotic/platelet antiaggregant thienopyridine derivs. II (R = H, CO₂R₁; R₁ = C₁-4 alkyl; X = H, halo), was prepared Thus, reaction of thiophene-2-carboxaldehyde with ClCH₂CO₂CHMe₂ in Me₂CHOH containing Me₂CHONa at 20 , with workup and vacuum distillation, gave 93% I. Saponification of I and reaction with NH₂OH.HCl (may also be performed in situ with preparation) gave 95% 2-thienylacetaldoxime, which underwent hydrogenation to the amine (91.5%), conversion to the formimine (100%), and cyclization (93%) to give 4,5,6,7-tetrahydrothieno[3,2-c]pyridine-HCl. This underwent neutralization (100%) and benzylation with 2-ClC₆H₄CH₂Cl (83%) to give ticlopidine-HCl, i.e. II-HCl (R = H, X = 2-Cl). Preparation of clopidogrel-H₂SO₄ is also described.

STN

70

Search for references showing obviousness of a substance claimed as a biosequence

- Conduct a similarity search in REGISTRY, DGENE, PCTGEN
 - BLAST®, FASTA
- Conduct a pattern match search in REGISTRY
 - Family sequence search (/SQFP)
 - Subsequence search (/SQSP)
 - Combined family and subsequence search (/SQSFP)
- Absent other differences, substances having highly similar sequences may carry an expectation of similar function

STN

71

Searching for prior art evidence of obviousness based on a biosequence

Search Question:

What prior art earlier than 2001 describes the use of human growth hormone-related proteins having the terminal sequence FPTIPLSRLF, followed by a gap of 1-10 amino acids, followed by the sequence RLHQLAFDTYQE, for the treatment of diabetes?

STN

72

Overall Search Strategy

1. Search the sequence in REGISTRY as a subsequence family pattern match search
2. Crossover the answer set to HCAPLUS to find the corresponding publications
3. Refine the answer set using the therapeutic use (THU) CAS Role and limiting to diabetes
4. Limit the answer set to prior art by publication year
5. Display results

STN

73

String search the peptide sequence in REGISTRY

```
=> FILE REGISTRY
=> S ^FPTIPLSRLF.{1,10}RLHQLAFDITYQE/SQSFP
L1      1108 ^FPTIPLSRLF.{1,10}RLHQLAFDITYQE/SQSFP
```

- The ^ symbol requires that the string FPTIPLSRLF is at the beginning of the sequence.
- The .{1,10} indicates the presence of a gap of from one to ten amino acids when the query sequence is aligned with candidate answer sequences in the file.
- The qualifier /SQSFP indicates a protein sequence search that permits functionally similar amino acids. The query sequence may or may not be embedded in larger sequences.

• <http://www.cas.org/support/stngen/stndoc/sequences.html>

STN

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Search HCAPLUS to take advantage of CAS Roles and search term cost savings

```
=> FILE HCAPLUS

=> S L1/THU
      1623 L1
      879011 THU/RL
L2      667 L1/THU
        (L1 (L) THU/RL)

=> S L2 AND PY<2001
      20924137 PY<2001
L3      344 L2 AND PY<2001

=> S L3 AND DIABETES
      123718 DIABETES
L4      12 L3 AND DIABETES
```

12 records published before 2001 are identified which describe substances having the query sequences and which may be linked to treatment of diabetes.

<http://www.cas.org/support/stngen/grc/index.html>

STN

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D KWIC shows Keywords in Context

```
=> D L4 KWIC 10

L4 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
SO Acta Diabetologica (1995), 32(2), 131-4
   CODEN: ACDAEZ; ISSN: 0940-5429
ST insulin dependent diabetes IGF1 somatotropin
IT Diabetes mellitus
   (insulin-dependent, effect of recombinant human growth hormone
   treatment on insulin-like growth factor (IGF-I) levels in
   insulin-dependent diabetic patients)
IT 12629-01-5, Human growth hormone
   RL: BAC (Biological activity or effector, except adverse); BSU
   (Biological
   study, unclassified); THU (Therapeutic use); BIOL (Biological
   study); USES (Uses)
   (effect of recombinant human growth hormone on insulin-like growth factor
   levels in insulin-dependent diabetic patients)
```

D KWIC is an efficient way of browsing answer sets for relevant answers. LOGOFF HOLD to review the displayed answers in the transcript before resuming the search.

STN

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Publication date show record is prior art

=> D L4 9 IBIB ABS HITSEQ

L4 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:696651 HCAPLUS
 DOCUMENT NUMBER: 127:355665
 TITLE: Use of growth hormone for treatment of primary insulin resistance syndrome and abdominal obesity
 INVENTOR(S): Johannsson, Gudmundur; Marin, Per; Lonn, Lars; Ottosson, Malin; Stenlof, Kaj; Bjorntorp, Per; Sjostrom, Lars; Bengtsson, Bengt-ake
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Ab, Swed.; Johannsson, Gudmundur; Marin, Per; Lonn, Lars; Ottosson, Malin; Stenlof, Kaj; Bjorntorp, Per; Sjostrom, Lars; Bengtsson, Bengt-Ake
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738709	A1	19971023	WO 1997-SE601	19970410 <--
CA 2250907	A1	19971023	CA 1997-2250907	19970410 <--
AU 9724190	A	19971107	AU 1997-24190	19970410 <--
EP 935469	A1	19990818	EP 1997-919856	19970410 <--

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HITSEQ shows REGISTRY sequence

AB The invention relates to the use of growth hormone, preferably human growth hormone or analogs thereof for the manufg. of a medicament for treatment of individuals with the primary insulin resistance syndrome. They include individuals with abdominal/visceral obesity and its metabolic and circulatory consequences including insulin resistance, lipoprotein aberrations and hypertension. The medicament is also used to increase insulin sensitivity and for treatment and prevention of non-insulin dependent **diabetes** mellitus.

IT **12629-01-5**, Human growth hormone
 RL: BAC (Biological activity or effector, except adverse); BSI (Biological study, unclassified); THU (T study); USES (Uses)
 (growth hormone for treatment of primary insulin resistance syndrome and abdominal obesity)

RN 12629-01-5 HCAPLUS
 CN Somatotropin (human) (9CI) (CA INDEX NAME)

SEQ
 1 FPTIPLSRFL DNAMLAHRL HQLAFDTYQE FEEAYIPKEQ KYSFLQNPQT
 51 SLCFSESIPT PSNREETQOK SNLELLRISL LLIQSWLEPV QFLRSVFANS
 101 LVYGASDSNV YDLLKDLEEG IQTLMGRLLED GSPRTGQIFK QTYSKFDTNS
 151 HND DALLKNY GLLYCFRKDM DKVETFLRIV QCRSVEGSCG F

The HITSEQ display shows which sequences in the source document match the query sequence, in the context of the publication information.

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Tips for more comprehensive obviousness searches

- Use the **Index** feature to identify relevant files to search; search in multifile files, including business and meetings files
- Search multiple categories of patents, e.g., design patents, plant patents, reissue patents, statutory invention registrations, etc. (USPATFULL, IFIPAT)
- Search for defensive publications (RD, CAplus), grant applications (PROMT, NLDB) and theses (DISSABS)

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Tips for more comprehensive obviousness searches

- Search in full-text files for substance, process and device details; use the **D KWIC** and **D BROWSE** display formats to evaluate answers (USPATALL, PCTFULL, EPFULL, FRFULL, PATDPAFULL)
- Use the US NCL, IPC, ECLA, and F-term classifications to identify patent references based on their technology classifications
- Add a patent family search (**FSEARCH**) to patent references found by topic or substance search; dates and disclosures may vary among patent family members

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Tips for more comprehensive obviousness searches

- Search CAS RNs in multiple bibliographic and full text files
- **TRANSFER** patent numbers from answer sets for searching in other files
- Use file-specific thesauri to find synonyms and alternative search terms (CAplus Lexicon)
- Use left truncation and simultaneous left and right truncation to capture search term variations
- Set commands
 - **SET PLURALS ON**
 - **SET ABB ON**

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Summary

- Searching for prior art evidence to evaluate obviousness focuses on finding
 - Multiple references which can be combined to describe the claimed invention
 - Information suggesting a reason to combine the reference teachings or that “teach away” from the invention
 - Information that address secondary considerations
- Use STN tools and features to help you conduct more comprehensive obviousness searches

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Need Help?

- Patent Information on STN
<http://www.cas.org/support/stngen/stndoc/patent.html>
- STN E-Seminar Archive
https://casevents.webex.com/casevents/onstage/tool/record/archives.php?productmenu=PRO_STN&frommenu=1&Rnd=1619391779&Rnd=1408568032
- Obviousness
– MPEP 2141
http://www.uspto.gov/web/offices/pac/mpep/mpep_e8r5_2100.pdf
- CAS Customer Care
1-800-753-4227

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STN[®]: Searching for Patent Prior
Art Evidence of Obviousness