

2021 – Opposition/Validity/Novelty Search - Biotech/Life Sciences Sample Answer

[This document exemplifies how to interpret the search request, the preparation and gathering keywords and patent classes and conducting a sample search including comments of how and why using search statements.]

Consider that the date is January 2018, you work for a search agency and have received the following request from one of your regular clients.

Please conduct a validity search against a granted EP patent claiming:

1. A detection procedure to diagnose rheumatoid arthritis (RA) in a protein-containing synovial fluid comprising

- (a) deposition of a sample onto a well plate, glass slide or nitrocellulose platform,
- (b) contacting the deposited sample with an antibody against CD93,
- (c) further contacting the deposited sample with a secondary antibody conjugate marker and a solution comprising a chromogenic solution, and
- (d) comparing of the chromogenic signal for the sample with a control to determine if CD93 expression level is higher than that of the control.

2. The procedure according to claim 1, wherein the chromogenic substrate solution is OPD (ophenylenediamine).

3. The procedure according to claims 1 or 2, where the secondary antibody marker is gold or horseradish peroxidase.

The client informs you that use of gold as a marker is of particular interest.

The front page of the granted EP claims priority dates of 20.01.2009 and 25.10.2009

With any opposition the 1st thing I would want to do is discuss the patent with my patent attorney. In this case my attorney has already directed to a simplified version of the granted claims 1, 5 and 4. I would still check with my attorney whether it would be sufficient to limit the scope of some of these claims. I note that the final date for an opposition would be July 2018

Features of interest

Timeframe of interest

Two priority dates – this should be addressed, as it cannot be known which priority dates the claims are entitled to. It is always best to work with the latest possible date.

The search should therefore cover:

- Patent/non-patent publications published prior to 25.10.2009
- EP/WO publications (with a later EP filing) filed before 25.10.2009 may also be of interest.

I would also look up the EPO file wrapper for this patent as this might tell me:

- If the patent is entitled to its priority date, or if it relies on material added later in the priority year;
- More information about the actual invention behind the claims

If the patent has to rely on a later date for its priority this gives an additional period within which I can find relevant prior art.

The invention itself may give me additional search terms or even alternative search questions to help me find useful prior art.

I have not had time to check the file wrapper so I will assume that the patent is only entitled to claim priority from its filing date of 18.01.2010. This means that would replace 20091025 with 20100118 as my search limits.

For shorthand below, I have used "APD<20100118" to cover options.

The <u>technical features</u> of interest:

- RA treatment
- Use of anti-CD93 antibodies in diagnostics (the well plate material is probably not a key point)
- The test is using synovial fluid; that may be a rare fluid to use.
- Chromogenic labelling can be a limiting feature; the second antibody suggests this may be a sandwich assay, although this isn't specified
- Use of gold as a marker is important (from the client's instructions); this can therefore be used
- The chromogenic substrate of claim 2 is not a requirement; it is unclear how important this specific option is, but it may be useable as a focussing feature.
- The other secondary antibody marker of claim 3 may be of use as a secondary focus; based on the instructions given, this secondary focus can be limited to the peroxidase.

Search Strategy Preparation 1: Understand science:

For new areas I start with broad google searches.

"anti-cd93" or "cd93 antibody" give a few good leads.

Expanding to include diagnostics found <u>The characterization of a novel monoclonal antibody against CD93</u> <u>unveils a new antiangiogenic target (nih.gov)</u> reading the introduction looks like it would useful to help my understanding.

Looking for RA antibody treatment I quickly found a few articles including the recent <u>Monoclonal Antibodies in Rheumatoid Arthritis (medscape.com)</u> And the earlier more general <u>Antibody therapy for rheumatoid arthritis - PubMed (nih.gov)</u>

Sometimes I find the wiki entry on a subject be helpful <u>Rheumatoid arthritis - Wikipedia</u> especially in identifying alternative synonyms or broader descriptions that could be used instead of RA.

The use of gold was flagged as significant so I also for "gold Rheumatoid arthritis" which lead me directly to <u>Gold salts - Wikipedia</u> and to a specific salt Sodium aurothiomalate. See <u>Sodium aurothiomalate - Wikipedia</u> for CAS Registry Number 12244-57-4 and a few synonyms.

Search Strategy Preparation 2: Identify classifications:

IPC headings can be very broadly defined in this subject area; the CPC has additional more narrowly subheadings, and thus offers a better focus for initial searches.

The patent will have CPCs assigned; some may be of interest. In this case, there are a large number of CPCs (from Espacenet): A61K31/7105 (EP,US); A61P1/00 (EP); A61P1/04 (EP); A61P1/16 (EP); A61P1/18 (EP); A61P11/00 (EP); A61P11/02 (EP); A61P11/02 (EP); A61P11/02 (EP); A61P13/12 (EP); A61P17/00 (EP); A61P17/02 (EP); A61P19/02 (EP); A61P19/02 (EP); A61P21/00 (EP); A61P25/00 (EP); A61P25/04 (EP); A61P25/06 (EP); A61P27/02 (EP); A61P29/00 (EP); A61P31/04 (EP); A61P31/10 (EP); A61P31/12 (EP); A61P31/14 (EP); A61P35/00 (EP); A61P37/08 (EP); A61P43/00 (EP); A61P9/10 (EP); G01N33/6893 (EP,US); G01N2333/70596 (EP,US);

It is known that A61P relates to Medicinal Preparations against particular conditions, and the range of headings from CPC covers most of the section.

As the claim is focussed more on the diagnostic/detection process, the G01N headings are more relevant, and the initial strategies can be focussed there.

Definitions:

•	G01N 33/00	Investigating or analysing materials by specific methods not covered by groups $\underline{\text{G01N 1/00}}$ - $\underline{\text{G01N 31/00}}$
	G01N 33/48	 Biological material, e.g. blood, urine (<u>G01N 33/02</u>, <u>G01N 33/26</u>, <u>G01N 33/44</u>, <u>G01N 33/46</u> take precedence); Haemocytometers (counting blood corpuscules distributed over a surface by scanning the surface <u>G06M 11/02</u>)
	G01N 33/50	 Chemical analysis of biological material, e.g. blood, urine; Testing involving biospecific ligand binding methods; Immunological testing (measuring or testing processes involving enzymes or microorganisms, compositions or test papers therefor; processes for forming such compositions, condition responsive control in microbiological or enzymological processes <u>C12Q</u>)
	G01N 33/68	••• involving proteins, peptides or amino acids {(involving lipoproteins G01N 33/92)}
	G01N 33/6893	••••{related to diseases not provided for elsewhere}
	G01N 33/6896	••••• {Neurological disorders, e.g. Alzheimer's disease}
1	G01N 2333/00	Assays involving biological materials from specific organisms or of a specific nature
	G01N 2333/435	from animals; from humans
	G01N 2333/705	Assays involving receptors, cell surface antigens or cell surface determinants
	G01N 2333/705	••• Molecules with a "CD"-designation not provided for elsewhere in G01N 2333/705
•	G01N 33/00	Investigating or analysing materials by specific methods not covered by groups $\underline{G01N \ 1/00}$ - $\underline{G01N \ 31/00}$
	G01N 33/48	 Biological material, e.g. blood, urine (<u>G01N 33/02</u>, <u>G01N 33/26</u>, <u>G01N 33/44</u>, <u>G01N 33/46</u> take precedence); Haemocytometers (counting blood corpuscules distributed over a surface by scanning the surface <u>G06M 11/02</u>)
	G01N 33/50	 Chemical analysis of biological material, e.g. blood, urine; Testing involving biospecific ligand binding methods; Immunological testing (measuring or testing processes involving enzymes or microorganisms, compositions or test papers therefor; processes for forming such compositions, condition responsive control in microbiological or enzymological processes C12Q)
	G01N 33/53	•••Immunoassay; Biospecific binding assay; Materials therefor

G01N 33/564 •••• for pre-existing immune complex or autoimmune disease {, i.e. systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, rheumatoid factors or complement components C1-C9}

A check shows that there are no other subheadings of G01N233/705 relating to CD93, and therefore **G01N2333/70596** is a good prospect. The parent heading **G01N2333/705** may also be pertinent. However 2333/ headings are indexing headings only, and are indexing codes, and may not be comprehensive.

G01N33/6893 is vaguely defined but also should be considered.

One or more of the A61P headings will cover RA, and should be noted; headings in A61P19/ and A61P 29/ look most appropriate from the CPC definitions.

Search Strategy Preparation 3: Keywords:

Each search point can have synonyms which should be considered. CD93:

• There are a number of synonym terms for CD93; the Wikipedia page https://en.wikipedia.org/wiki/CD93 gives:

CD93, C1QR1, C1qR(P), C1qRP, CDw93, ECSM3, MXRA4, dJ737E23.1, CD93 molecule, cluster of differentiation 93

• The Background section of the target patent gives other terms of potential use

This term is uncommon in the two G01N CPCs above (a full text search on PatBase for CD_93).

Search options not including CD93

The search can also be targeted at the remaining points:

- RA
- Synovial fluid as source
- Chromogenic labelling of a secondary antibody marker
- Gold as a secondary antibody marker

Search Strategy Creation

Using just CD93 as a search term, there are not that many cases identified: Full text search (SC= IPC or CPC):

• *sc*=(*g*01*n*, *a*61*p*) and *aft*=*cd*_"93" and *apd*<20100118 128 families on PatBase SC= search in any Patent Classification codes – IPC, CPC, Japanese F-terms or US National codes , means OR here

AFT = full text search for the phrase cd93 or cd 93, aft allows for machine translated text into English APD = application date - < = earlier than date

Title/abstract/claims search:

• *sc*=(*g*01*n*, *a*61*p*) and *ATAC*=*cd*_"93" and *apd*<20100118 17 families on PatBase ATAC = searching Title, Abstracts and Claims, allows for machine translated text into English

These numbers suggest that the searches for CD93 can be conducted broadly (Search Option 1).

Additionally, it may be possible to extend the searches to cover a later period than the APD used, and use the additional records as sources for <u>citation searches</u> (**Search Option 1a**)

Search options not including CD93

The search can also be targeted at the remaining points:

- RA
- Synovial fluid as source
- Chromogenic labelling of a secondary antibody marker
- Gold as a secondary antibody marker

As noted above, G01N relates to detection processes.

It is best to run multiple options at different levels of broadness/keywords. These sets can then be combined/focussed further if appropriate. The following table has options for the full range of CPC G01N, the specific headings identified from the target patent, and a broader option for G01N2333/70596; only title/abstract/claims fields have been searched at this time.

1A	cpc=g01n and atac=(rheumatoid arthrit*) and apd< 20100118	1,601
1B	cpc=g01n33/6893 and atac=(rheumatoid arthrit*) and apd< 20100118	206
1C'	cpc=g01n2333/705* and atac=(rheumatoid arthrit*) and apd< 20100118	228
1C	cpc=g01n2333/70596 and atac=(rheumatoid arthrit*) and apd< 20100118	29
1D	cpc=g01n33/564 and atac=(rheumatoid arthrit*) and apd<20100118	407

1E	Combination with OR of 1B and 1D	552
2A	cpc=g01n and atac=(synovial*, (knee w5 fluid*)) and apd< 20100118	743
2B	cpc=g01n33/6893 and atac=(synovial*, (knee w5 fluid*)) and apd< 20100118	81
2C	cpc=g01n2333/70596 and atac=(synovial*, (knee w5 fluid*)) and apd< 20100118	11
2D	cpc=g01n33/564 and atac=(synovial*, (knee w5 fluid*)) and apd< 20100118	115
ЗA	cpc=g01n and atac=chromogen* and apd< 20100118	1,827
3B	cpc=g01n33/6893 and atac=chromogen* and apd< 20100118	48
3C	cpc=g01n2333/70596 and atac=chromogen* and apd< 20100118	7
3D	cpc=g01n33/564 and atac=chromogen* and apd< 20100118	13

CPC = just CPC codes

G01N = broad code for INVESTIGATING OR ANALYSING MATERIALS BY DETERMINING THEIR CHEMICAL OR PHYSICAL PROPERTIES. This gives all patent documents where the analysis is linked to RA

* = unlimited truncation, also phrase in bracket is searched as this ie anything with the stem RHEUMATOID ARTHRIT

1C' is a broader search selection than 1C that specifically limits to "assays involving molecules with a CD designation"

There is some overlap between 1B and 1D but that most are unique to either approach it would probably be better to look at one set and then use the NOT operator to remove duplicates from the second set. This is the only really safe way that a NOT can be used in most searches ATAC=(knee w5 fluid*) retrieves items where the terms KNEE and FLUID* can be separated up to 5 other terms. W5 is a proximity operator that doesn't specify which term comes 1st in the hit document. Search 3A is much too broad for this request.

Browsing at 3C:

1) US2012039911 AA

CD93 OR USE OF SOLUBLE FRAGMENT THEREOF

2) US2009202429 AA METHODS FOR TESTING ANTI-THROMBOTIC AGENTS

3) US2010062450 AA

METHODS AND KITS FOR EARLY DETECTION OF CANCER OR PREDISPOSITION THERETO

4) US2007020179 AA

ACUTE LEUKEMIA AND LYMPHOBLASTIC LYMPHOMA-SPECIFIC CD43 EPITOPE AND USE THEREOF

5) US6261790 BA

MONOCLONAL ANTIBODIES AND ANTIBODY COCKTAIL FOR DETECTION OF PRION PROTEIN AS AN INDICATION OF TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES

6) US2003021792 AA TISSUE-SPECIFIC ENDOTHELIAL MEMBRANE PROTEINS

7) US6264940 BA

RECOMBINANT POLIOVIRUS FOR THE TREATMENT OF CANCER Item 1 is the patent to be opposed. None of the other 6 families are related in any way to RA. I believe it is quite unlikely the any of the 3 Searches will find additional useful documents.

From the above, options are as follows:

• In Sets 1D, 2B, 2C and 2D some/all of these documents can be reviewed in full (Search Option 2)

Combination of 3A with either of 1A {28 hits} or 2A {25 hits} is readily possible as a very general attempt to retrieve more generic disclosures (Search Option 3)

Initial search for named chemicals

* * * * * * * * * Welcome to STN International * * * * * * * * * * FILE 'HOME' ENTERED AT 17:55:55 ON 27 JUL 2021 => file reg FILE = command to change database in this case to the CAS Registry database FILE 'REGISTRY' ENTERED AT 17:56:15 ON 27 JUL 2021 => s 12244-57-4 S = search commandBy default just entering a CAS Reg No will retrieve the required chemical as this forms part of the Basic Index for this database L11 12244-57-4 (12244-57-4/RN) => d rn cn str D = display command Here displaying the Reg No, the chemical names associated with this compound (only 1^{st} 50 for multi-posted compounds and if available a structure diagram. ANSWER 1 OF 1 REGISTRY COPYRIGHT 2021 ACS on STN Г1 RN **12244-57-4** REGISTRY CN Butanedioic acid, 2-mercapto-, gold(1+) sodium salt (1:1:?) (CA INDEX NAME) OTHER CA INDEX NAMES: Butanedioic acid, mercapto-, monogold(1+) sodium salt (9CI) CN OTHER NAMES: Aurolate CN Aurothiomalate sodium CN CN Chrysothios Gold sodium thiomalate CN Kidon CN CN Miocrisina CN Myochrysin CN Myochrysine CN Myocrisin CN Shiosol CN Sodium aurithiomalate CN Sodium aurothiomalate CN Tauredon



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

=> e	Auranofin/cn
E = e	expand from specified index command.
Withc	out a suffix this would go to the Basic Index but here with /CN it shows the
full	names from the Chemical Name field
E1	1 AURANAMIDE/CN
E2	1 AURANETIN/CN
EЗ	1> AURANOFIN/CN
E4	1 AURANOMIDE A/CN
E5	1 AURANOMIDE B/CN
E6	1 AURANOMIDE C/CN
E7	1 AURANSTEROL/CN
E8	1 AURANTHIN/CN
E9	1 AURANTHINE/CN
E10	3 AURANTIA/CN
E11	1 AURANTIACIN/CN
E12	1 AURANTIACIN, DIACETATE/CN
=> s	e3
This	retrieves the specific entry from the Expanded list
L2	1 AURANOFIN/CN
=> d	rn cn str
- 0	
L2	ANSWER I OF I REGISTRY COPYRIGHT 2021 ACS ON STN
RN	34031-32-8 REGISTRY
CN	Gold, [1-(thiokappa.S)-B-D-glucopyranose
	2,3,4,6-tetraacetato](triethylphosphine) - (CA INDEX NAME)
OTHER	R CA INDEX NAMES:
CN	β-D-Glucopyranose, 1-thio-, 2,3,4,6-tetraacetate, gold complex
CN	Gold, (I-thio-B-D-glucopyranosato)(triethylphosphine)-,
~~~	2,3,4,6-tetraacetate (8CI)
CN	Gold, $(1-thio-\beta-D-glucopyranose)$
	2, 3, 4, 6-tetraacetato-S) (triethylphosphine) -
CN	[1-(Thiokappa.S)-β-D-glucopyranose
	2,3,4,6-tetraacetato](triethylphosphine)gold
OTHER	R NAMES:
CN	AKTI
CN	Auranofin
CN	
CN	
CN	GOLQ SALL
CN	
CN	Kloaura Dideesee
CN	Klaauran
CN	SKF 39102
CN	SKE 3910ZU
CN	[(Tetra-O-acety1-β-D-g1ucopyranosy1)tnio](triethy1phosphine)gold



Absolute stereochemistry shown **PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

=> e Cd93/cn

E1	1	CD92 (ANTIGEN) (HUMAN KG1A CELL)/CN
E2	1	CD92 (ANTIGEN) (HUMAN PRECURSOR)/CN
EЗ	0	> CD93/CN
E4	1	CD93 (ANTIGEN) (HUMAN CLONE VIMD2)/CN
E5	1	CD93 ANTIGEN (HUMAN SOLUBLE EXTRACELLULAR DOMAIN SCD93)/CN
ЕG	1	CD93 ANTIGEN (HUMAN SOLUBLE EXTRACELLULAR DOMAIN)/CN
E7	1	CD93 ANTIGEN (HUMAN)/CN
E8	1	CD94 (ANTIGEN) (CHIMPANZEE GENE CD94)/CN
E9	3	CD94 (ANTIGEN) (HOLSTEIN-FRIESIAN CATTLE MONONUCLEAR CELL GE
		NE KLRD1)/CN
E10	1	CD94 (ANTIGEN) (MOUSE STRAIN C57BL/6 REDUCED)/CN
E11	1	CD94 (ANTIGEN) (MUS MUSCULUS STRAIN C57BL/6 GENE CD94)/CN
E12	1	CD94 (ANTIGEN) (ORANGUTAN MONONUCLEAR CELL GENE CD94*01)/CN
=> s	e4-e7	
Here	have selec	ted a range of entries 4-7 from this list
	1	"CD93 (ANTIGEN) (HUMAN CLONE VIMD2)"/CN
	1	"CD93 ANTIGEN (HUMAN SOLUBLE EXTRACELLULAR DOMAIN SCD93)"/CN
	1	"CD93 ANTIGEN (HUMAN SOLUBLE EXTRACELLULAR DOMAIN)"/CN
	1	"CD93 ANTIGEN (HUMAN)"/CN
L3	4	("CD93 (ANTIGEN) (HUMAN CLONE VIMD2)"/CN OR "CD93 ANTIGEN (HUMAN
		SOLUBLE EXTRACELLULAR DOMAIN SCD93)"/CN OR "CD93 ANTIGEN (HUMAN
		SOLUBLE EXTRACELLULAR DOMAIN)"/CN OR "CD93 ANTIGEN (HUMAN)"/CN)
=> d	rn cn 1-4	
т.3	ANGWER 1 (	NE 4 RECISTRY COPYRIGHT 2021 ACS on STM
RN	1783902-67	Z-9 REGISTRY
CN	Cd93 antic	(CA
CIN	TNDEX NAME	
ОТНЕБ	NAMES.	1/
CN	1. PN. KB1	526307 SEOID. 1 claimed protein
CIN	1. 11. 11.1	SZOSO, SEQID. I Claimed protein
L3	ANSWER 2 C	OF 4 REGISTRY COPYRIGHT 2021 ACS on STN
RN	1238920-82	-5 REGISTRY
CN	Cd93 antig	<b>jen (human)</b> (CA INDEX NAME)
OTHER	NAMES:	
CN	3: PN: WO2	2010087594 SEQID: 33 claimed protein

ANSWER 3 OF 4 REGISTRY COPYRIGHT 2021 ACS on STN L3 1238920-81-4 REGISTRY RN CN Cd93 antigen (human soluble extracellular domain) (CA INDEX NAME) OTHER NAMES: 1: PN: WO2010087594 SEQID: 1 claimed protein CN ANSWER 4 OF 4 REGISTRY COPYRIGHT 2021 ACS on STN т.З RN 403779-05-5 REGISTRY CN Complement C1q receptor (human clone VIMD2) (9CI) (CA INDEX NAME) OTHER NAMES: CN CD93 (antigen) (human clone VIMD2) Here items 2 and 4 are the most useful compounds for this search => LOG HOLD Log hold disconnects the online session but allows the searcher to return to the same place in this session within the next 2 hours STN INTERNATIONAL SESSION SUSPENDED AT 18:02:41 ON 27 JUL 2021 * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * SESSION RESUMED IN FILE 'REGISTRY' AT 18:22:08 ON 27 JUL 2021 FILE 'REGISTRY' ENTERED AT 18:22:08 ON 27 JUL 2021

# Non-patent literature

Non-patent literature searches can be conducted through available resources, using combinations of keywords as appropriate.

The following sources are likely to be promising:

- MEDLINE/PubMed
- Chemical Abstracts
- Google Scholar (allows some full text searching)
- DeepDyve (allows some full text searching)

#### **Citation-based searches**

The target record, and records located by the initial searches, can be mined for citations (forward and backward) and optionally a second stage (citations on the citations – this will usually require classification/limitation). (Search Option 4)

Medline/PubMed includes its own indexing system.

The Medical Subject Headings (MeSH) thesaurus which a controlled and hierarchically-organized vocabulary.

Medical Subject Headings - Home Page (nih.gov)

Although these won't me used in this search due to limited time one possible heading that could be included in any future search is <u>Monitoring</u>, <u>Immunologic MeSH Descriptor Data</u>

# Monitoring, Immunologic MeSH Descriptor Data 2022

Details	Qualifiers	MeSH Tree Structures Concepts
N	leSH Heading	Monitorina Immunologic
Tr	ee Number(s)	E01.370.225.812.505
		E01.370.520.505
		E05.200.812.505
		E05.478.594.550
	Unique ID	D015166
RDF Uni	ique Identifier	http://id.nlm.nih.gov/mesh/D015166
	Annotation	determ of immune status of patient in diag, and ther: do not confuse entry term IMMUNOSURVEILLANCE with IMMUNOLOGIC SURVEILLANCE, a
		function of T-lymphocytes; IM GEN only; avoid indexing routinely every word "monitoring" as "monitoring": read MeSH definition
	Scope Note	Testing of immune status in the diagnosis and therapy of cancer, immunoproliferative and immunodeficiency disorders, and autoimmune abnormalities.
		Changes in immune parameters are of special significance before, during and following organ transplantation. Strategies include measurement of tumor
		antigen and other markers (often by RADIOIMMUNOASSAY), studies of cellular or humoral immunity in cancer etiology, IMMUNOTHERAPY trials, etc.
	Entry Version	MONITORING IMMUNOL
	Entry Term(s)	Immune Monitoring
		Immunologic Monitoring
		Immunosurveillance
		Monitoring, Immune
		Monitoring, Immunological
		Monitoring, Radioimmunologic
		Monitoring, Radioimmunological
Drov	ious Indexing	Radiominunologic Montoling
Flev	ious indexing	Immunosuppression (1577-1500)
		Immunuture apy (15/4-1500) Monitoria Dhysiologic (1976-1989)
		Monitoring, Enyslologic (1970-1900)

#### It is also possible that there may be useful MESH headings within the hierarchy at <u>Antibodies MeSH</u> <u>Descriptor Data</u>

#### Antibodies MeSH Descriptor Data 2022

Details	Qualifiers	MeSH Tree Structures Concepts
м	leSH Heading	Antibodies
Tr	ee Number(s)	D12.776.124.486.485.114
		D12.776.124.790.651.114
		D12.776.377.715.548.114
	Unique ID	D000906
RDF Uni	que Identifier	http://id.nlm.nih.gov/mesh/D000906
	Annotation	antibodies to IMMUNOGLOBULIN A; IMMUNOGLOBULIN G; etc. = ANTIBODIES, ANTI-IDIOTYPIC (IM) + IMMUNOGLOBULIN A; IMMUNOGLOBULIN
		G; etc. (IM); ANTIBODY-TOXIN CONJUGATES is available as toxin carrier: see note there
	Scope Note	Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the ANTIGEN (or a very similar shape) that
		induced their synthesis in cells of the lymphoid series (especially PLASMA CELLS).
	Pharm Action	Immunologic Factors
Reg	istry Number	0
NLM CI	assification #	QW 575
	See Also	Antigen-Antibody Reactions
Entry	Combination	biosynthesis:Antibody Formation
		deficiency:Immunologic Deficiency Syndromes

# In this search I will not use MESH headings as I do not have time. Continuing after the earlier LOG HOLD in STN

FILE 'REGISTRY' ENTERED AT 18:22:08 ON 27 JUL 2021 COPYRIGHT (C) 2021 American Chemical Society (ACS)

COST	IN EUROS		SINCE FILE	TOTAL
			ENTRY	SESSION
FULL	ESTIMATED	COST	64,29	64,39

```
=> S 11-12
Combining the 2 possible gold antibody markers
L4 2 (L1 OR L2)
```

=> file hcaplus, Medline This command has now opened 2 databases at the same time Medline and a version of the Chemical Abstracts database

FILE 'HCAPLUS' ENTERED AT 18:23:07 ON 27 JUL 2021 FILE 'MEDLINE' ENTERED AT 18:23:07 ON 27 JUL 2021 => s rheumatoid(1a)arthrit? This is searching the Basic index of both databases. (1a) means that the 2 terms can be in any order with up to 1 word between them. ? is a truncation sign allowing for any additional characters after the search string ARTHRIT 236532 RHEUMATOID(1A) ARTHRIT? т.б => s rheumatoid##(1a)arthrit? Forgot about the possible use of "rheumatoidal" each # is a truncation sign allowing for 1 or no further characters т.7 236559 RHEUMATOID##(1A) ARTHRIT? => S diagnos? 6400323 DIAGNOS? Г8 => s 17 and 18 Combination of RA with diagnosis like terms 48890 L7 AND L8 Ц9 => e identificn Using the Expand command to check if there are any common abbreviations for IDENTIFICATION or RECEGNOSIS etc. IDENTIFICITY/BI Е1 1 IDENTIFICKATSII/BI E2 1 0 --> IDENTIFICN/BI E3 34 IDENTIFICO/BI E4 24 E5 IDENTIFICOU/BI 1 IDENTIFICSTION/BI E6 1 IDENTIFICTATION/BI E7 27 IDENTIFICTION/BI Ε8 E9 1 IDENTIFICTIONS/BI 1 E10 IDENTIFICVATION/BI 1 E11 IDENTIFICY/BI 1 E12 IDENTIFICYING/BI => e recogn 2 RECOGIZE/BI E1E2 4 RECOGIZED/BI 10 --> RECOGN/BI EЗ Ε4 1 RECOGNABILITY/BI Е5 1 RECOGNAISED/BI ЕG 10 RECOGNAN/BI E7 1 RECOGNASED/BI Ε8 22 RECOGNATION/BI Ε9 1 RECOGNATIVE/BI 1 1 2 E10 RECOGNAZIBLE/BI RECOGNAZING/BI E11 E12 RECOGNE/BI => e 2 RECOGNETION/BI E13 E14 1 RECOGNEYES/BI 14 RECOGNI/BI E15 1 RECOGNI9TION/BI E16 3 RECOGNIATION/BI E17 1 RECOGNIAZATION/BI E18 E19 1 RECOGNIBILITY/BI

E20	2	RECOGNICE/BI
E21	1	RECOGNICER/BI
E22	3	RECOGNIDA/BI
E23	1	RECOGNIDON/BI
E24	3	RECOGNIED/BI
=> e		
E25	1	RECOGNIES/BI
E26	1	RECOGNIFION/BI
E27	1	RECOGNIGION/BI
E28	4	RECOGNIION/BI
E29	1	RECOGNIITION/BI
E30	1	RECOGNIMD/BI
E31	199	RECOGNIN/BI
E32	2	RECOGNIN // BI
E33 E24	1	RECOGNINATION/BI
E34 E35	⊥ 110	RECOGNINITION/ BI
E36	1	RECOGNINTION/BI
=> @		
E37	1	RECOGNINZE/BI
E38	1	RECOGNION/BI
E39	33	RECOGNISABILITY/BI
E40	1599	RECOGNISABLE/BI
E41 E42	33	RECOGNISABLY/BI
E42 E13	1	RECOGNISALBE/BI
E43 E44	2	RECOGNISANCE/BI
E45	7	RECOGNISATION/BI
E46	10636	RECOGNISE/BI
E47	1	RECOGNISEBE/BI
E48	39018	RECOGNISED/BI
=> S me	asur? or ic	dentification or recogni? or detect?
L10 1	7557594 MEA	ASUR? OR IDENTIFICATION OR RECOGNI? OR DETECT?
=> s 17	and 110	
Related	terms to I	DIAGNOSIS combined with RA
L11	56897 L7	AND L10
=> s 19	or 111	
L12	88900 L9	OR L11
=> S (c Produce L13	d93 or cd() d very few 18 (CI	93)(1a)(anti()bod? or antibod?) <mark>hits!</mark> D93 OR CD(W) 93)(1A)(ANTI(W) BOD? OR ANTIBOD?)
=> s (c	d93 or cd()	93)
L14	504 (CI	093 OR CD(W) 93)
=> s an	ti()bod? oı	r antibod?
L15	2175228 AN	II(W) BOD? OR ANTIBOD?
=> s l1	4(p)115	
Used th ANTIBOD	e proximity IES	$\gamma$ operator P (in the same paragraph) to link CD93 and
L16	65 L14	4(P) L15

=> d hit Ths display command shows which part of the 1st record was retrieved by search L16 L16 ANSWER 1 OF 65 HCAPLUS COPYRIGHT 2021 ACS on STN Antibodies and Immunoglobulins ΤТ RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (CD93 inhibitors for use in treatment of cancer) => s 15 2 L5 T.17 => s 116-117 66 (L16 OR L17) L18 => s 112 and 118 Nothing found here combining RA "diagnosis" with CD93 antibodies 0 L12 AND L18 L19 => file reg FILE 'REGISTRY' ENTERED AT 18:30:45 ON 27 JUL 2021 => sel name 14 The SEL NAME command creates set included the chemical names of L4 (the gold antibodv markers) E1 THROUGH E25 ASSIGNED => file hcaplus, medline FILE 'HCAPLUS' ENTERED AT 18:31:14 ON 27 JUL 2021 FILE 'MEDLINE' ENTERED AT 18:31:14 ON 27 JUL 2021 => s e1-e25 Search for the contents of the SEL NAME command 6210 ("((TETRA-O-ACETYL-.BETA.-D-GLUCOPYRANOSYL)THIO)(TRIETHYLPHOSPHI L20 NE)GOLD"/BI OR "(1-(THIO-.KAPPA.S)-.BETA.-D-GLUCOPYRANOSE 2,3,4, 6-TETRAACETATO) (TRIETHYLPHOSPHINE)GOLD"/BI OR AKTIL/BI OR AURANO FIN/BI OR AUROLATE/BI OR "AUROTHIOMALATE SODIUM"/BI OR CHRYSOTHI OS/BI OR CRISINOR/BI OR CRISOFIN/BI OR "GOLD SALT"/BI OR "GOLD SODIUM THIOMALATE"/BI OR KIDON/BI OR MIOCRISINA/BI OR MYOCHRYSIN /BI OR MYOCHRYSINE/BI OR MYOCRISIN/BI OR "NSC 321521"/BI OR RIDA URA/BI OR RIDAURAN/BI OR SHIOSOL/BI OR "SKF 39162"/BI OR "SKF 39162D"/BI OR "SODIUM AURITHIOMALATE"/BI OR "SODIUM AUROTHIOMALA TE"/BI OR TAUREDON/BI) => s 14 4083 L4 T.21 => s 120-121 and 112 548 (L20 OR L21) AND L12 L22 => s 123 not p/dt Looking for non-patent documents - where P/DT = document type patent L23 519 L22 NOT P/DT

=> s	123 and p	y<2010
Limit	ing to pu	blications before 2010 - really should have used PY<2011 to allow
for t	the extra	year - see page 1-2 above
L24	467	L23 AND PY<2010
=> sa	ave temp B	P1/a 124
SAVE	TEMP save	s the results of a search (at no charge) for 14 days
ANSWE	ER SET L24	HAS BEEN SAVED AS 'BP1/A'
=> d	hist full	
This	displays	the complete search strategy in full
		TORDAL DURDED DE 10.01.15 ON 07 THE 0001
т.1	FILE 'REG	1STRY' ENTERED AT 18:01:15 ON 27 JUL 2021 1 SFA 12244-57-4
ТТ		E AURANOFIN/CN
L2		1 SEA AURANOFIN/CN
		E CD93/CN
L3		4 SEA ("CD93 (ANTIGEN) (HUMAN CLONE VIMD2)"/CN OR "CD93 ANTIGEN
		(HUMAN SOLUBLE EXTRACELLULAR DOMAIN SCD93)"/CN OR "CD93
		ANTIGEN (HUMAN SOLUBLE EXTRACELLULAR DOMAIN)"/CN OR "CD93
		ANTIGEN (HUMAN)"/CN)
		D CLUSTER
		D SET
L4		2 SEA (L1 OR L2)
		SEL NAME L4
Г2		Z SEA 1238920-82-5 OR 403779-05-5
	FILE 'HCA	PLUS, MEDLINE' ENTERED AT 18:23:07 ON 27 JUL 2021
L6	23653	2 SEA RHEUMATOID(1A) ARTHRIT?
L7	23655	9 SEA RHEUMATOID##(1A) ARTHRIT?
L8	640032	3 SEA DIAGNOS?
L9	4889	0 SEA L7 AND L8
		E IDENTIFICN
		E RECOGN
L10	1755759	4 SEA MEASUR? OR IDENTIFICATION OR RECOGNI? OR DETECT?
L11	5689	7 SEA L7 AND L10
L12	8890	0 SEA L9 OR L11
L13	1	8 SEA (CD93 OR CD(W) 93) (IA) (ANTI(W) BOD? OR ANTIBOD?)
LL4 T15	50	4 SEA (CD93 OR CD(W) 93)
LLS T1C	21/522	8 SEA ANTI(W) BOD? OR ANTIBOD?
ПΤ0	C	
т.17		2 SFA 15
шт, т.1.8	6	6 SEA (L16 OR L17)
L19	0	0 SEA L12 AND L18
-		
	FILE 'REG	ISTRY' ENTERED AT 18:30:45 ON 27 JUL 2021
		SEL NAME L4
	FILE 'HCA	PLUS MEDITNE' ENTERED AT 18.31.14 ON 27 JUL 2021
T-2.0	621	0 SEA ("((TETRA-O-ACETYL-, BETA, -D-GLUCOPYRANOSYL)THIO)(TRIETHYLPH
-	-	OSPHINE)GOLD"/BI OR "(1-(THIOKAPPA.S)BETAD-GLUCOPYRANOSE
		2,3,4,6-TETRAACETATO) (TRIETHYLPHOSPHINE)GOLD"/BI OR AKTIL/BI
		OR AURANOFIN/BI OR AUROLATE/BI OR "AUROTHIOMALATE SODIUM"/BI
		OR CHRYSOTHIOS/BI OR CRISINOR/BI OR CRISOFIN/BI OR "GOLD
		SALT"/BI OR "GOLD SODIUM THIOMALATE"/BI OR KIDON/BI OR
		MIOCRISINA/BI OR MYOCHRYSIN/BI OR MYOCHRYSINE/BI OR MYOCRISIN/B
		I OR "NSC 321521"/BI OR RIDAURA/BI OR RIDAURAN/BI OR SHIOSOL/BI
		OR "SKF 39162"/BI OR "SKF 39162D"/BI OR "SODIUM AURITHIOMALATE
		"/BI OR "SODIUM AUROTHIOMALATE"/BI OR TAUREDON/BI)
L21	408	3 SEA L4
⊥∠∠ тор	54	O SEA (LZU UK LZI) AND LIZ
цар Т.24	51 46	7 SEA L23 AND PY<2010
	10	

SAVE TEMP BP1/A L27

=> DUP REM 124 This should remove any duplicate publications found in set L24 - the Chemical Abstracts references should be retained PROCESSING COMPLETED FOR L24 L25 425 DUP REM L24 (42 DUPLICATES REMOVED)

=> SAVE TEMP BP1a/A L25

ANSWER SET L25 HAS BEEN SAVED AS 'BP1A/A'

=> d 125 ti 1-10 Now would display all titles to identify any possible further leads. Here have just displayed the  $1^{st}$  10 documents.

- L25 ANSWER 1 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN DUPLICATE 1 TI An evidence-based assessment of the clinical significance of drug-drug interactions between disease-modifying antirheumatic drugs and non-antirheumatic drugs according to rheumatologists and pharmacists
- L25 ANSWER 2 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN
- TI Risk factors for the development of gastric mucosal lesions in **rheumatoid arthritis** patients receiving long-term nonsteroidal anti-inflammatory drug therapy and the efficacy of famotidine obtained from the FORCE study
- L25 ANSWER 3 OF 425 MEDLINE ® on STN
- TI Effect of disease modifying anti-rheumatic drugs on radiographic progression in **rheumatoid arthritis**.
- L25 ANSWER 4 OF 425 MEDLINE  $\ensuremath{\mathbb{R}}$  on STN
- TI Disability measured by the modified health assessment questionnaire in early rheumatoid arthritis: prognostic factors after two years of follow-up.
- L25 ANSWER 5 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN
- TI Guidelines for the use of conventional and newer disease-modifying antirheumatic drugs in elderly patients with **rheumatoid arthritis**
- L25 ANSWER 6 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN DUPLICATE 2 TI Promiscuous Interaction between Gold-Specific T Cells and APCs in Gold Allergy
- L25 ANSWER 7 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN TI Non-biologic disease modifying antirheumatic drugs
- L25 ANSWER 8 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN TI Antirheumatic drugs for RA
- L25 ANSWER 9 OF 425 MEDLINE ® on STN TI Pemphigus and chrysotherapy: all that glitters is not gold!.
- L25 ANSWER 10 OF 425 HCAPLUS COPYRIGHT 2021 ACS on STN DUPLICATE 3
  TI Tuning the Au(I)-mediated inhibition of cathepsin B through ligand
  substitutions

#### **Run out of time**