

# **5th Annual Global TechMining Conference**

## **Methodology for Identifying Pharmaceutical Key Molecules Using Technology Foresight of Patent Documents**

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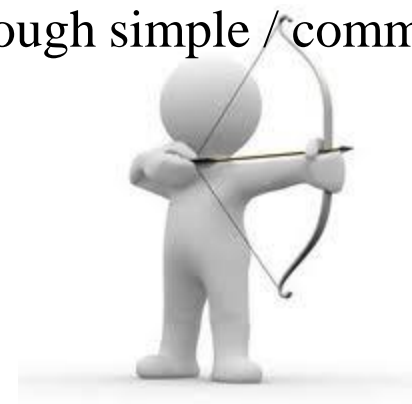
16/09/2015

# Introduction – Some data of Pharmaceutical Industry

- Global pharmaceutical sales reached an all-time high of approximately \$980 billion in 2013
  - However, the rate of growth declined in 2013 compared to 2012 due to the expiration of patent protection on a number of blockbuster drugs in markets dominated by generic equivalent
- The number of New Molecular Entities (NMEs) launched in 2013 was the third-highest in the last decade
- Pharmaceutical R&D is a difficult and expensive process in an industry with high expectations

# Introduction

- Technology race
  - R&D of new process of synthesis and formulations related to drugs/medicines
- Analysis of synthesis process using patent documents to identify key substances
  - Substances (intermediate) structurally similar to the drug of interest
  - Critical precursors for the preparation of the final product
  - Compound that is converted to the final product through simple / common synthetic routes



# Document Patents

The pharmaceutical sector is one of the sectors that most protects its inventions using document patents



high costs incurred in the R&D of new products

# Typical Claims of Patents Relating to Pharmaceutical Inventions

- Product (API)
- **Processes**
- Formulations and compositions
- Combinations
- Dosage/Dose
- Salts, Ethers and esters
- Polymorphs
- Markush Claims
- Method of treatment
- Use claims (including second use)

# Technology Assessment based on Document Patent

- Contains descriptions of scientific and technical concepts as well as practical details of processes
- Conveys the most recent information
- Has a fairly uniform structure
- Contains information which is not divulged in any other form of literature
- Covers most of what is new and most of what is worthwhile knowing about technological development

# **Methodology for Identifying Pharmaceutical Key Substances**

# The Methodology – 6 STEPS

1. Searches for the process patents
2. Selects the process patents that explains the synthesis route
3. Identifies all the reagents and intermediates present in the routes patented
4. Selects the most frequently substances present in the routes patented
5. Compares the chemical structures of the most frequently cited substances with the API (drug)
  - Select the similar
6. Seeks producers/suppliers of the substances that are most structurally similar to the API (drug)
  - Selects the ones that have producers/suppliers



# Exemplifying the Methodology

Case Study

AIDS/HIV/ARVs

Zidovudine – first ARV

# Case Study - Zidovudine

## ➤ AIDS

- First diagnosed in 1981 in the USA
- Disease that affects about 35 million people worldwide (2012)



## ➤ Caused by infection with the human immunodeficiency virus (HIV)

- There is currently no cure or effective HIV vaccine

## ➤ Treatment consists of highly active antiretroviral therapy

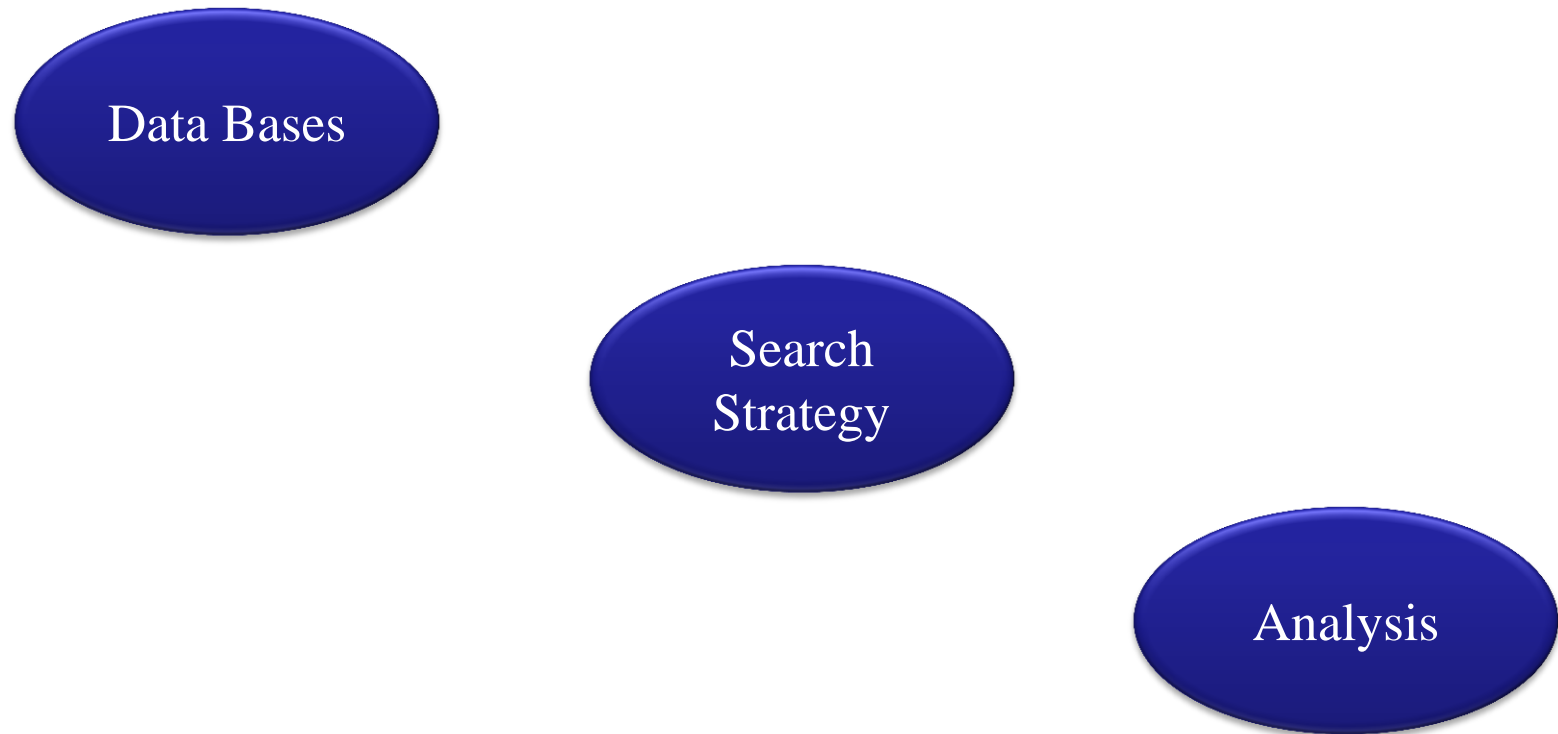
## ➤ There are 25 ARVs used in AIDS treatment in world

- 88 drugs in developing phase
  - Searches for more effective drugs
  - Improved tolerability
  - Reducing side effects
  - Dosing simplification



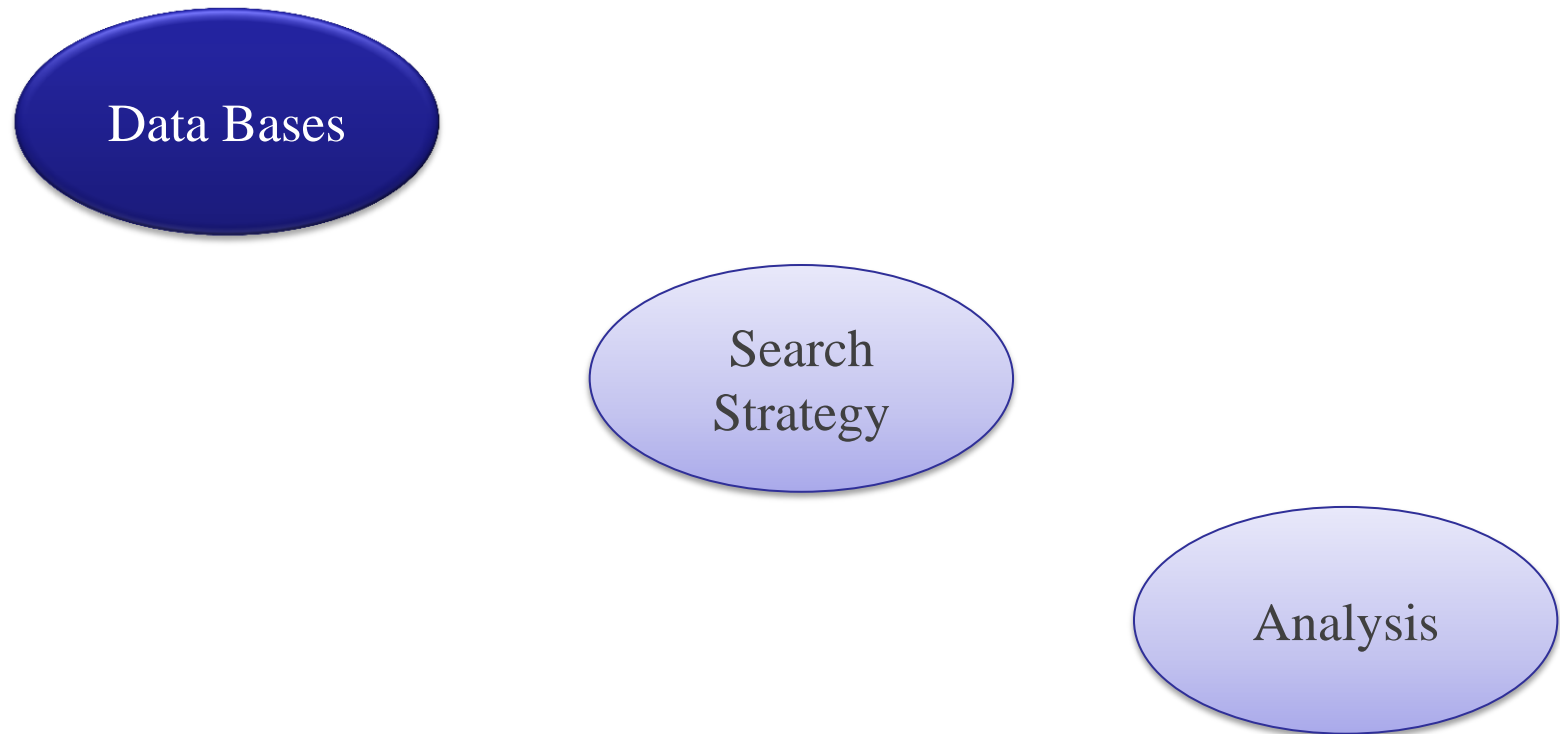
# Technology Assessment based on Document Patent

- Main steps of the technology assessment



# Technology Assessment based on Document Patent

- Main steps of the technology assessment



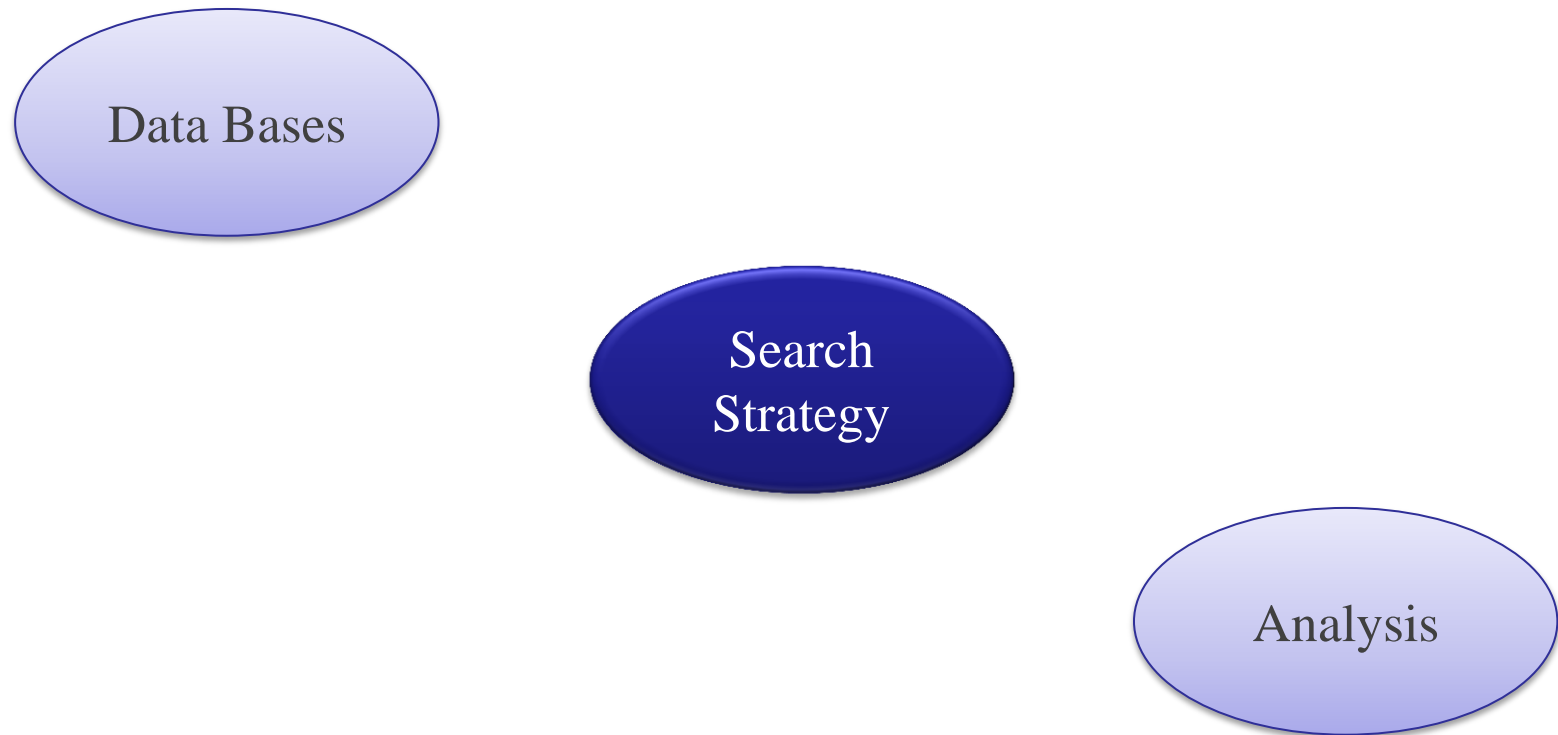
# Technology Assessment based on Document Patent

## ➤ SciFinder Scholar®

- Internationally recognized database
- Facilitates the retrieval of patent application – by API
- Contains filter that enable only document for the synthesis of the API
- Allows to select the documents with detailed production route

# Technology Assessment based on Document Patent

- Main steps of the technology assessment



## Steps 1 and 2 of the Methodology

1. Search for the process patents
2. Select the process patents that explain the synthesis route

# Search for the process patents and Select the process patents that explain the synthesis route

## – STEPS 1 and 2

The screenshot displays the SciFinder web application interface. At the top, the browser address bar shows the URL <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf>. The SciFinder logo is on the left, and navigation links for 'Preferences', 'SciFinder Help', and 'Sign Out' are on the right. A 'Welcome Flavia Mendes' message is also present.

The main navigation bar includes 'Explore', 'Saved Searches', and 'SciPlanner'. The 'Explore' section is active, showing a search area titled 'SUBSTANCES: SUBSTANCE IDENTIFIER'. A text input field contains 'zidovudine', which is circled in blue. A callout bubble points to this field with the text 'Zidovudine'. Below the input field, there are examples of identifiers: '50-00-0', '999815', and 'Acetaminophen'. A blue 'Search' button is located below the examples.

On the left sidebar, the 'SUBSTANCES' category is expanded, and 'Substance Identifier' is selected, also circled in blue. A callout bubble points to this selection with the text 'Substance Identifier'. Other categories visible include 'REFERENCES' (with sub-items like Research Topic, Author Name, etc.) and 'REACTIONS' (with sub-item Reaction Structure).

On the right sidebar, there are sections for 'SAVED ANSWER SETS' (showing 'Patentes - Sulfato de amonia') and 'KEEP ME POSTED' (showing 'You have no profiles.').

At the bottom, there is a footer with 'Contact Us | Legal' and 'Copyright © 2014 American Chemical Society. All Rights Reserved. | 京ICP备13013560号'.

# Search for the process patents and Select the process patents that explain the synthesis route

## – STEPS 1 and 2

The screenshot displays the SciFinder web interface. The browser address bar shows the URL <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf>. The SciFinder logo is in the top left, and the user is logged in as 'Welcome Flavia Mendes'. The main navigation bar includes 'Explore', 'Saved Searches', and 'SciPlanner'. A search for 'zidovudine' has been performed, resulting in one substance (30516-87-1). The 'Get Reactions' button is circled in red, and a callout bubble points to it with the text 'Get Reaction'. The 'Get Reactions' dialog box is open, showing options to retrieve reactions for all substances or selected substances, and to limit results by reaction role (Product, Reactant, Reagent, Reactant or reagent, Catalyst, Solvent, Any role). The dialog box has 'Get' and 'Cancel' buttons.

Substance Identifier "zidovudine" > substances (1) > 30516-87-1

Get References **Get Reactions** Get Commercial Sources Tools

Sort by: CAS Registry Number

0 of 1 Substance Selected

1. 30516-87-1

~9794 ~163

Absolute stereochemistry., Rotation (+).

$C_{10}H_{13}N_5O_4$   
Thymidine, 3'-azido-3'-deoxy-

Regulatory Information  
Spectra  
Experimental Properties

**Get Reactions**

Retrieve reactions for:

- ☒ All substances
- ☐ Selected substances

Limit results by reaction role:

- ☒ Product
- ☐ Reactant
- ☐ Reagent
- ☐ Reactant or reagent
- ☐ Catalyst
- ☐ Solvent
- ☐ Any role

Get Cancel



# Search for the process patents and Select the process patents that explain the synthesis route – STEPS 1 and 2

SciFinder®

Substance Identifier "zidovudine" (545)

REACTIONS

Analyze by: Document Type

Journal 450

Patent 95

Online Computer File 6

Document Type

Patent

0 of 545 Reactions Selected

1. View Reaction Detail Link

3 Steps Hover over any structure for more options.

~184

~167

~163

Overview

Steps/Stages

1.1 R:EtO<sub>2</sub>CN=NC<sub>2</sub>Et, R:PPh<sub>3</sub>, S:AcOEt, S:DMF, rt; 30 min, rt; 2 h, rt

2.1 R:NaN<sub>3</sub>, R:NH<sub>4</sub>Cl, S:DMF, 95-100 h

2.2 R:HCl, S:H<sub>2</sub>O, acidify

3.1 R:NaOH, S:H<sub>2</sub>O, 1 h, rt

3.2 R:NaOH, S:H<sub>2</sub>O, pH 5-6

Notes

1) incremental addition of DEAD and PPh<sub>3</sub>, Reactants: 2, Reagents: 6, Solvents: 3, Steps: 3, Stages: 5, Most stages in any one step: 2

References

Synthesis improvement of zidovudine

Quick View Full Text

By Yu, Yong et al

From Yingyong Huagong, 40(8), 1484-1485; 2011

2. View Reaction Detail Link

2 Steps Hover over any structure for more options.

~163

# Search for the process patents and Select the process patents that explain the synthesis route

## – STEPS 1 and 2

**Get References**

Substance Identifier "zidovudine" > substances (1) > get reactions (545) > keep analysis "Document Type" (95)

**REACTIONS**

Get References Tools

Analyze Refine

Analyze by: Document Type

Patent 95

Show More

0 of 95 Reactions Selected

1. View Reaction Detail Link

8 Steps Hover over: <https://scifinder.cas.org/scifinder/view/scifinder/>

**SciFinder**

Explore Saved Searches SciFinder

Analyze Refine Categorize

Sort by: Accession Number

0 of 21 References Selected

1. Method for preparing zidovudine and intermediate thereof

Quick View PatentPak

By Li, Jinliang; Zhao, Nan; Liu, Shu; Cheng, Fenghua; Xiong, Yuyou; Zhou, Chunfeng

From PCT Int. Appl. (2013), WO 2013067669 A1 20130516. | Language: Chinese, Database: CAPLUS

2. Method for preparing zidovudine and intermediate thereof

Quick View PatentPak

By Li, Jinliang; Zhao, Nan; Liu, Shu; Cheng, Fenghua; Xiong, Yuyou; Zhou, Chunfeng

From PCT Int. Appl. (2013), WO 2013067666 A1 20130516. | Language: Chinese, Database: CAPLUS

3. Preparation of zidovudine and its intermediate

Quick View Other Sources

By Li, Jinliang; Yan, Li

From Faming Zhuanli Shengqing Gongkai Shuomingshu (2009), CN 101376667 A 20090304. | Language: Chinese, Database: CAPLUS

4. An improved process for the preparation of thymidine derivative

Quick View PatentPak

By Gharpure, Milind Moreshwar; Deshpande, Vishnu Hari; Sonawane, Swapnil Panditrao; Mehta, Satish Ramanlal

From Indian Pat. Appl. (2007), IN 2005MU00091 A 20070921. | Language: English, Database: CAPLUS

5. Synthesis of neutral porphyrinyl nucleotides as prodrugs for use as anticancer and antiviral agents

Quick View Other Sources

Analyze by: Publication Year

Year	Count
1995	5
2013	2
1993	2
1992	2
2009	1
2007	1
2005	1
2004	1
2003	1
2002	1

Show More

Chemical structures: O=C[C@H](O)[C@@H](O)C and CC(C)[C@H](O)C(=O)N

# Results of STEPS 1 and 2

- 21 patent documents for the zidovudine production process
- 25 different synthesis route for zidovudine were identified
  - One patent may have more than one processes

# Technology Assessment based on Document Patent

## ➤ Main steps of the technology assessment

### Steps 3 to 6 of the Methodology

3. Identify all the reagents and intermediates present in the routes patented
4. Select the most frequently substances present in the routes patented
5. Compare the chemical structures of the most frequently cited substances with the API
6. Seek producers/suppliers of the substances that are most structurally similar to the API



Analysis

# **Step 3**

## **Identifies all the reagents and intermediates present in the routes patented**

# Identifies all the Reagents and Intermediates – Zidovudine – STEP 3

← → ↻ <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf> ☆ ☰

SciFinder® Preferences | SciFinder Help Sign Out

Welcome Flavia Mendes

Explore ▾ Saved Searches ▾ SciPlanner Link Save Print Export

Substance Identifier "zidovudine" > substances (1) > get reactions (545) > keep analysis "Document Type" (95) > reaction 94 (of 95)

REACTION DETAIL ⓘ Get Reference Detail Get Full Text Send to SciPlanner

Return Previous Next

**94. 2 Steps** *Hover over any structure for more options.*

Steps	Stages	Notes	Yield
<b>1</b>	1.1 R:Disodium carbonate, S:DMF 1.2 R:PPh <sub>3</sub> , R:N <sub>2</sub> (CO <sub>2</sub> CHMe <sub>2</sub> ) <sub>2</sub>	Reactants: 2, Reagents: 3, Solvents: 1, Steps: 1, Stages: 2	<b>64%</b>
<b>2</b>	2.1 R:NaN <sub>3</sub> , S:DMF 2.2 R:AcOH	Reactants: 1, Reagents: 2, Solvents: 1, Steps: 1, Stages: 2	<b>73%</b>

**SOURCE**

Preparation of AZT (3'-azido-3'-deoxythymidine) and related compounds  
 Czernecki, Stanislas; Valery, Jean Marc  
 Assignee Universite Pierre et Marie CURIE Paris VI, Fr.  
 1991

**PATENT INFORMATION**

May 15, 1991  
 EP 427587  
 A1

**NUMBER OF STEPS**

2

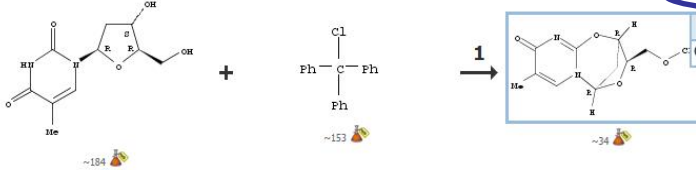
# Identifies all the Reagents and Intermediates – Zidovudine – STEP 3

SciFinder®

Substance Identifier "zidovudine" > substances (1) > get reactions (545) > keep analysis "Document Type" (95) > reaction 94 (of 95)

REACTION DETAIL

94. 2 Steps *Hover over any structure for more options.*



25442-42-6

CAS Registry Number: 25442-42-6

View Substance Detail

Explore by Structure

Synthesize this...

Get Reactions where Substance is a

Get Commercial Sources

Get Regulatory Information

Get References

Export as Image

Send to SciPlanner

Notes

Reactants: 2, Reagents:

Yield

64%

73%

Steps

Stages

1

1.1 R:Disodium carbonate, S:DMF

1.2 R:PPh<sub>3</sub>, R:N<sub>2</sub>(CO<sub>2</sub>CHMe<sub>2</sub>)<sub>2</sub>

2

2.1 R:NaN<sub>3</sub>, S:DMF

2.2 R:AcOH

SOURCE

Preparation of AZT (3'-azido-3'-deoxythymidine) and related compounds

Czernicki, Stanislas; Valery, Jean Marc

Assignee Universite Pierre et Marie CURIE Paris VI, Fr. 1991

PATENT INFORMATION

May 15, 1991

EP 427587

A1

NUMBER OF STEPS

2

# Identifies all the Reagents and Intermediates – Zidovudine – STEP 3

➤ Organizes the data – Example

API	Patent Number	Type of the Substance	Substances' CAS
Zidovudine	CN101376667	Reagent	67-56-1
	CN101376667	Reagent	533-67-5
	CN101376667	Intermediates	60134-26-1
	CN101376667	Reagent	98-59-9
	CN101376667	Intermediates	1133973-26-8
	CN101376667	Intermediates	1133973-41-7
	CN101376667	Intermediates	1133973-43-9
	CN101376667	Reagent	7288-28-0
	CN101376667	Intermediates	1133973-45-1
	CN101376667	Intermediates	1133973-47-3
	CN101376667	Intermediates	108441-90-3



## Results of Step 3

- 111 different molecules identified in 25 processes

### Step 4

**Selects the most frequently substances  
present in the routes patented**

# Selects the Most Frequently Substances – STEP 4

- 14 were present in more than one route

Substances' CAS		Number of times that it appears on the routes of synthesis
124-63-0	Mesyl chloride	7
50-89-5	Thymidine	5
7288-28-0		4
76-83-5		4
29706-84-1		3
104218-44-2		3
4234-08-6		2
134623-19-1		2
75-15-0		2
134485-36-2		2
99018-98-1		2
142741-93-3		2
2417-90-5		2
1463-10-1		2

## **Step 5**

**Compares the chemical structures of the 14 most frequently cited substances with the API**

# **Compares the Chemical Structures of the Zidovudine with the 14 Most Frequently Substances - STEP 5**

- Comparison of the structures



**Search similarity  
between the  
Zidovudine and  
the substances**

8 substances selected  
6 substances excluded

# Compares the Chemical Structures of the Zidovudine with the 14 Most Frequently Substances

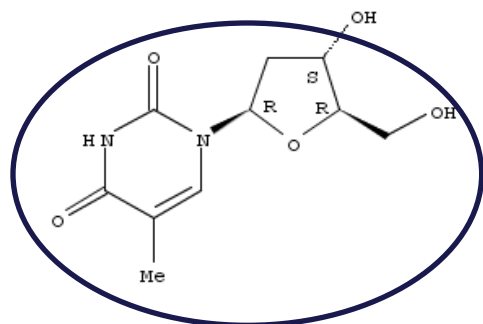
## - STEP 5

### ➤ Substance with structure similarity - Selected

Thymidine

CAS: 50-89-5

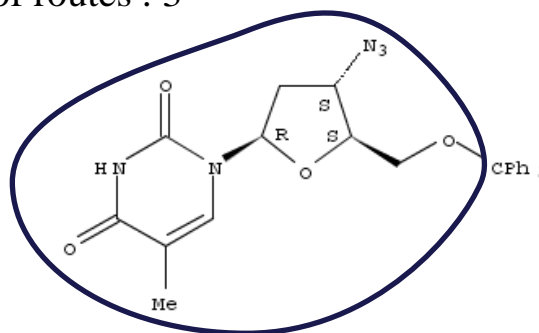
N. of routes: 5



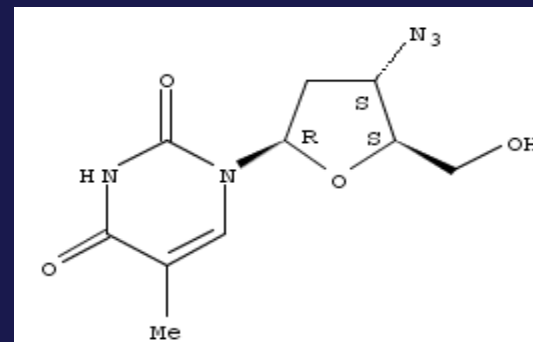
3'-azido-3'-deoxy-5'-O-(triphenylmethyl)- Thymidine

CAS: 29706-84-1

N. of routes : 3



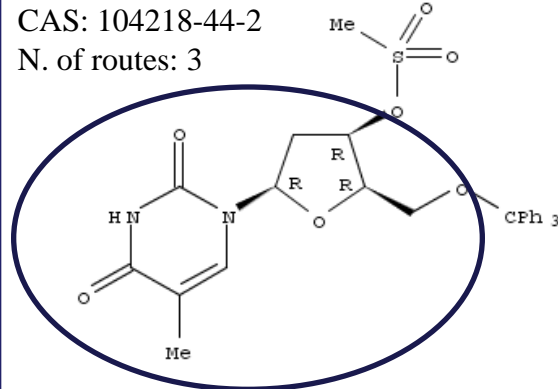
## ZIDOVUDINE



2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-3-O-(methylsulfonyl)-5-O-(triphenylmethyl)-β-D-threo-pentofuranosyl]-5-methyl-

CAS: 104218-44-2

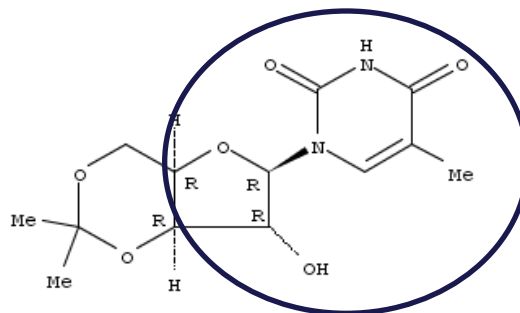
N. of routes: 3



5-methyl-1-[3,5-O-(1-methylethylidene)-β-D-xylofuranosyl]-2,4(1H,3H)-Pyrimidinedione

CAS: 4234-08-6

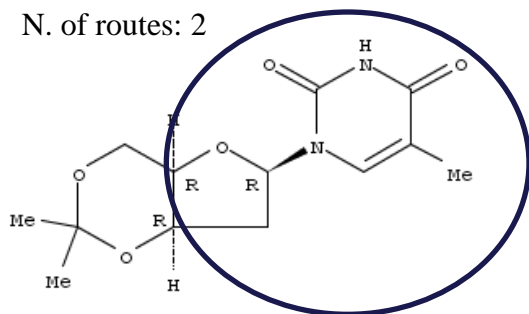
N. of routes: 2



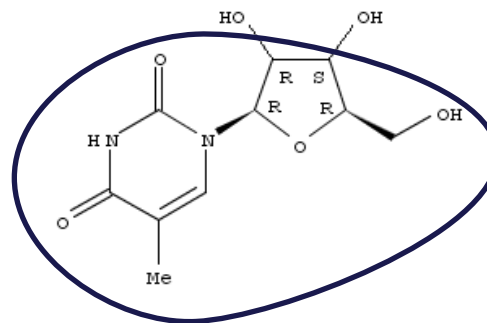
# Compares the Chemical Structures of the Zidovudine with the 14 Most Frequently Substances - STEP 5

## ➤ Substance with structure similarity - Selected

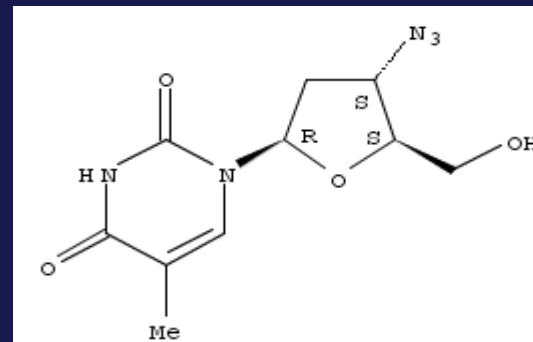
1-[2-deoxy-3,5-O-(1-methylethylidene)-b-D-threo-pentofuranosyl]-5-methyl-2,4(1H,3H)-Pyrimidinedione  
CAS: 99018-98-1  
N. of routes: 2



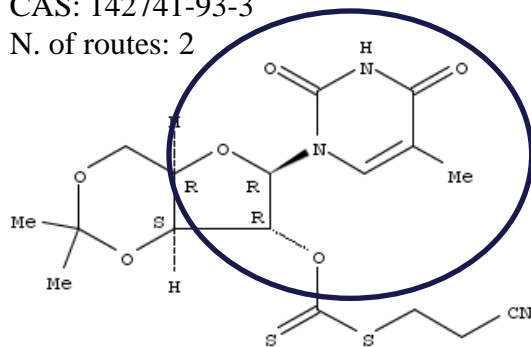
5-methyl- Uridine  
CAS: 1463-10-1  
N. of routes: 2



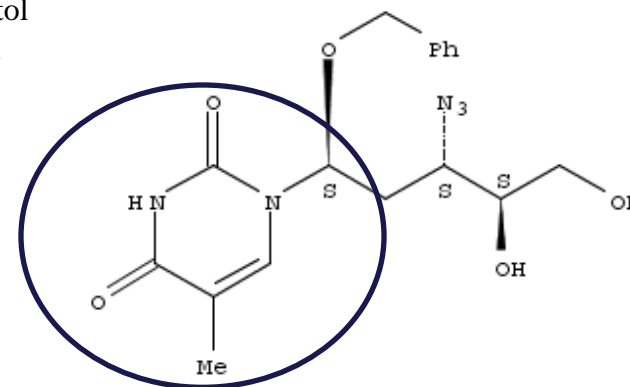
### ZIDOVUDINE



1-[2-O-[[2-cyanoethylthio]thioxomethyl]-3,5-O-(1-methylethylidene)-b-D-2,4(1H,3H)-Pyrimidinedione  
CAS: 142741-93-3  
N. of routes: 2



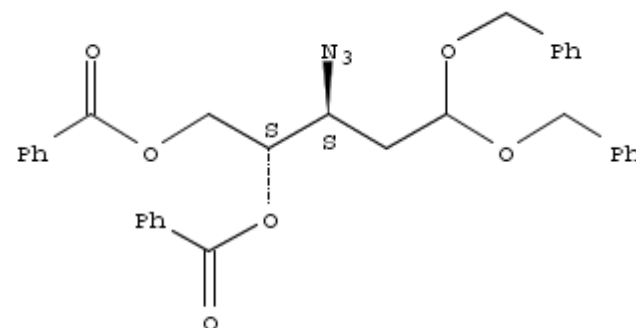
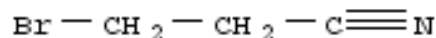
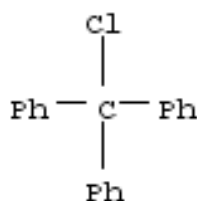
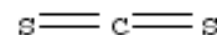
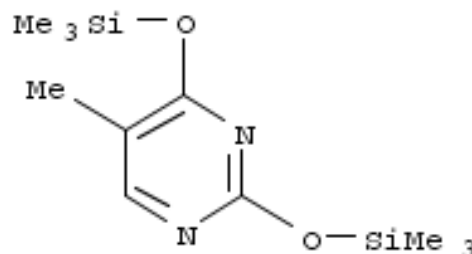
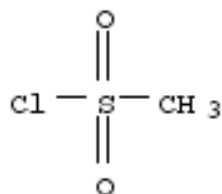
3-azido-2,3-dideoxy-1-C-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1-O-D-erythro-Pentitol  
CAS: 134623-19-1  
N. of routes: 2



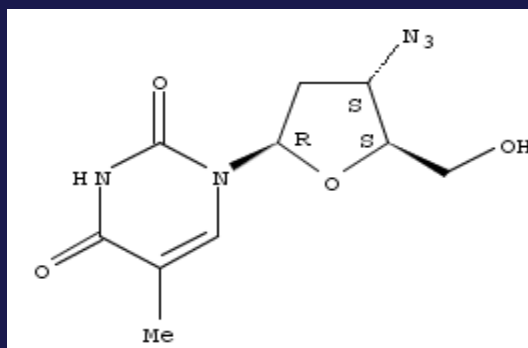
# Compares the Chemical Structures of the Zidovudine with the 14 Most Frequently Substances

## - STEP 5

- Substance without structure similarity - Excluded



### ZIDOVUDINE



## **Step 6**

**Seeks producers/suppliers of the substances that are most structurally similar to the API**



# Seeks Producers/Suppliers - STEP 6

- The commercial availability of key molecules may facilitate the synthesis
  
- Databases Example
  - Directory of World Chemical Producers (DWCP) of Chemical Info
  - Directory of Chemical Producers - Products of SRI Consulting
  - American Chemical Society (ACS)
  - Chemistry Industry Association of Canada, a International Council of Chemical Associations (ICCA)
  - Chinese Chemical Society
  - Indian Speciality Chemical Manufacturers' Association
  - SciFinder Scholar®

# Seeks Producers/Suppliers Using the SciFinder Scholar® - STEP 6

The screenshot displays the SciFinder Scholar web interface. The browser address bar shows the URL <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf>. The SciFinder logo is in the top left, and navigation links for 'Preferences', 'SciFinder Help', and 'Sign Out' are in the top right. A 'Welcome Flavia Mendes' message is also present. The main navigation bar includes 'Explore', 'Saved Searches', and 'SciPlanner'. On the left sidebar, the 'SUBSTANCES' section is active, with 'Substance Identifier' highlighted. The central search area is titled 'SUBSTANCES: SUBST' and contains a text input field with a list of CAS numbers: 50-89-5, 29706-84-1, 104218-44-2, 4234-08-6, and 99018-98-1. A callout bubble points to this list with the text 'Number of substances' CAS'. Below the input field, there are examples of search terms: 'Enter one per line.', 'Examples: 50-00-0', and 'aminophen'. A blue 'Search' button is located below the input field. Another callout bubble points to the 'Substance Identifier' option in the sidebar with the text 'Substance Identifier'. On the right sidebar, there are sections for 'SAVED ANSWER SETS' (listing 'Patentes - Sulfato de amonia' and 'Autosaved Reference Set') and 'KEEP ME POSTED' (stating 'You have no profiles.'). At the bottom, there is a footer with 'Contact Us | Legal' and 'Copyright © 2014 American Chemical Society. All Rights Reserved. | 京ICP备13013560号'.

Number of substances' CAS

Substance Identifier

SAVED ANSWER SETS ?

Patentes - Sulfato de amonia

Autosaved Reference Set

View All | Import

KEEP ME POSTED ?

You have no profiles.

Learn how to:

Create Keep Me Posted

Contact Us | Legal

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# Seeks Producers/Suppliers Using the SciFinder Scholar® - STEP 6

← → ↺ 🏠 <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf> ☆ ☰

**SUBSTANCES** ⓘ Get References Get Reactions Get Commercial Sources Tools ▾

Create Keep Me Posted Alert Send to SciPlanner

Analyze Refine Sort by: CAS Registry Number ▾ ⬇

0 of 8 Substances Selected

Display Options

Analyze by: ⓘ

Substance Role ▾

Preparation 8

Reactant or Reagent 8

Analytical Study 4

Formation, Nonpreparative 3

Process 3

Properties 3

Biological Study 2

Miscellaneous 2

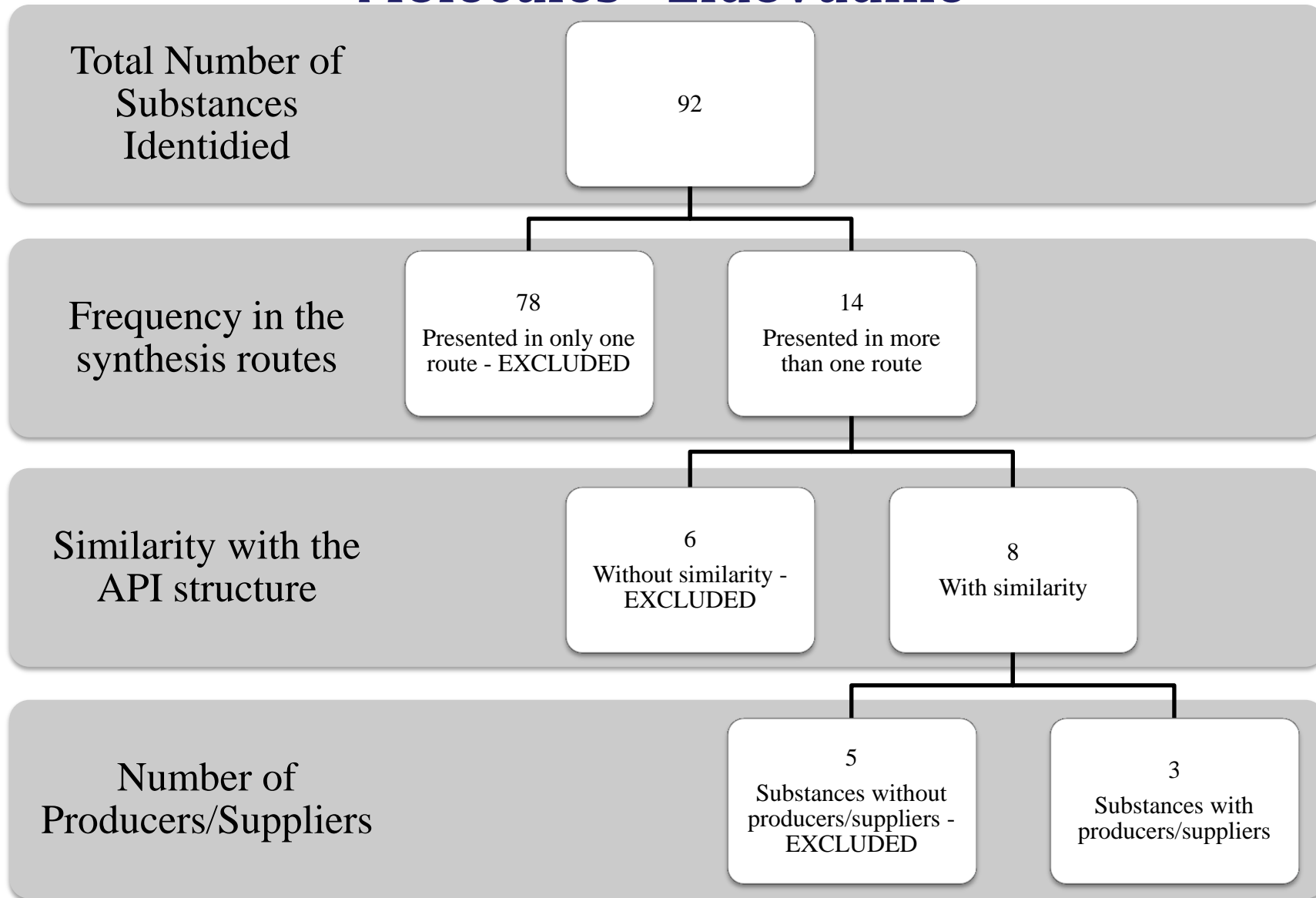
Occurrence 2

Prophetic in Patents 2

Show More

<p>1. <b>142741-93-3</b> ⓘ</p> <p>~3  </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>17</sub> H<sub>21</sub> N<sub>3</sub> O<sub>6</sub> S<sub>2</sub></b>            2,4(1<i>H</i>,3<i>H</i>)-Pyrimidinedione, 1-[2-<i>O</i>-[(2-cyanoethyl)thio]thioxomethyl]-3,5-<i>O</i>-(1-methylethylidene)-β-<i>D</i>-xylofuranosyl]-5-methyl-</p>	<p>2. <b>134623-19-1</b> ⓘ</p> <p>~3  </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>17</sub> H<sub>21</sub> N<sub>5</sub> O<sub>5</sub></b>  <i>D</i>-<i>erythro</i>-Pentitol, 3-azido-2,3-dideoxy-1-<i>C</i>-(3,4-dihydro-5-methyl-2,4-dioxo-1(2<i>H</i>)-pyrimidinyl)-1-<i>O</i>-(phenylmethyl)-, (1<i>S</i>)-</p>	<p>3. <b>104218-44-2</b> ⓘ</p> <p>~32  </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>30</sub> H<sub>30</sub> N<sub>2</sub> O<sub>7</sub> S</b>            2,4(1<i>H</i>,3<i>H</i>)-Pyrimidinedione, 1-[2-deoxy-3-<i>O</i>-(methylsulfonyl)-5-<i>O</i>-(triphenylmethyl)-β-<i>D</i>-<i>threo</i>-pentofuranosyl]-5-methyl-</p> <p>Regulatory Information</p>	<p>4. <b>99018-98-1</b> ⓘ</p> <p>~15  </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>13</sub> H<sub>18</sub> N<sub>2</sub> O<sub>5</sub></b>            2,4(1<i>H</i>,3<i>H</i>)-Pyrimidinedione, 1-[2-deoxy-3,5-<i>O</i>-(1-methylethylidene)-β-<i>D</i>-<i>threo</i>-pentofuranosyl]-5-methyl-</p>
<p>5. <b>29706-84-1</b> ⓘ</p> <p>~53    </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>29</sub> H<sub>27</sub> N<sub>5</sub> O<sub>4</sub></b>            Thymidine, 3'-azido-3'-deoxy-5'-<i>O</i>-(triphenylmethyl)-</p> <p>Regulatory Information Experimental Properties</p>	<p>6. <b>4234-08-6</b> ⓘ</p> <p>~13  </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>13</sub> H<sub>18</sub> N<sub>2</sub> O<sub>6</sub></b>            2,4(1<i>H</i>,3<i>H</i>)-Pyrimidinedione, 5-methyl-1-[3,5-<i>O</i>-(1-methylethylidene)-β-<i>D</i>-xylofuranosyl]-</p> <p>Experimental Properties</p>	<p>7. <b>1463-10-1</b> ⓘ</p> <p>~1083    </p> <p>Absolute stereochemistry.,Rotation (+).</p> <p><b>C<sub>10</sub> H<sub>14</sub> N<sub>2</sub> O<sub>6</sub></b>            Uridine, 5-methyl-</p> <p>Regulatory Information Spectra Experimental Properties</p>	<p>8. <b>50-89-5</b> ⓘ</p> <p>~10940    </p> <p>Absolute stereochemistry.</p> <p><b>C<sub>10</sub> H<sub>14</sub> N<sub>2</sub> O<sub>5</sub></b>            Thymidine</p> <p>Regulatory Information Spectra Experimental Properties</p>

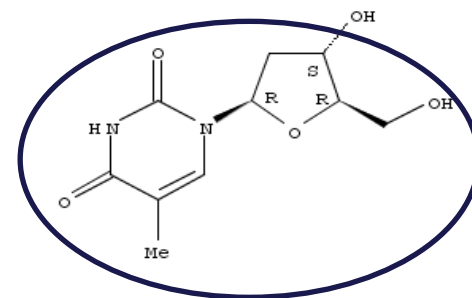
# Methodology for Identifying Pharmaceutical Key Molecules - Zidovudine



# Key Molecules of Zidovudine Using the Methodology

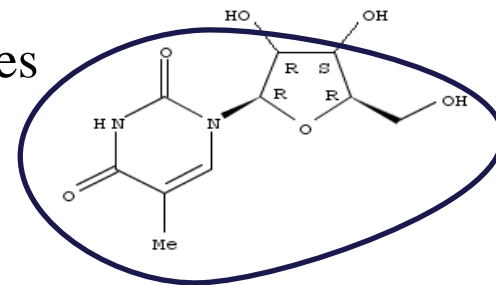
## ➤ Thymidine: 50-89-5

- Present in 5 routes of synthesis – different assignees
- First patent in 1958 (public domain)
- 187 international producers/suppliers



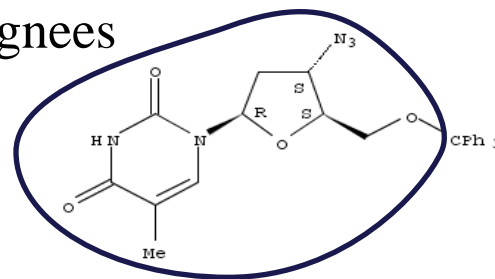
## ➤ 5-Methyl-Uridine: 1463-10-1

- Present in 2 routes of synthesis – different assignees
- First patent in 1962 (public domain)
- 111 international producers/suppliers



## ➤ 3'-azido-3'-deoxy-5'-O-(triphenylmethyl)-Thymidine: 29706-84-1

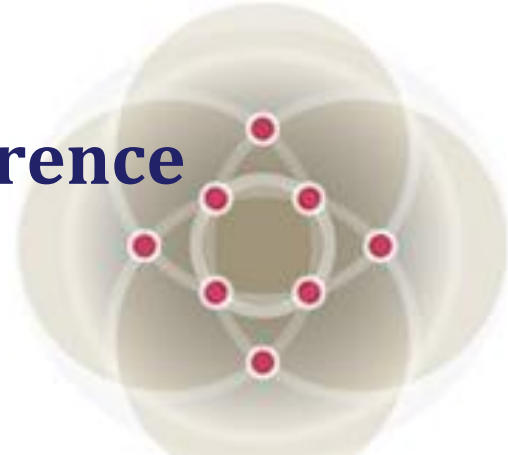
- Present in 3 routes of synthesis – different assignees
- First patent in 1957 (public domain)
- 8 international producers/suppliers



# Conclusions

- Analysis of synthesis patents
  - All substances (reagents, intermediates products) can be identified
- The comparison between the molecular structure of the API and the substances that most appears in route of synthesis allows:
  - The selection of more complexity substances
- It is possible to use the methodology to identify key molecules in a group of API's
- Other analysis can be done:
  - Temporal evaluation of the patents
  - Identify the key assignees
  - Relation between the assignees and the substances

# 5th Annual Global TechMining Conference



## Methodology for Identifying Pharmaceutical Key Molecules Using Technology Foresight of Patent Documents

**THANKS!!!**

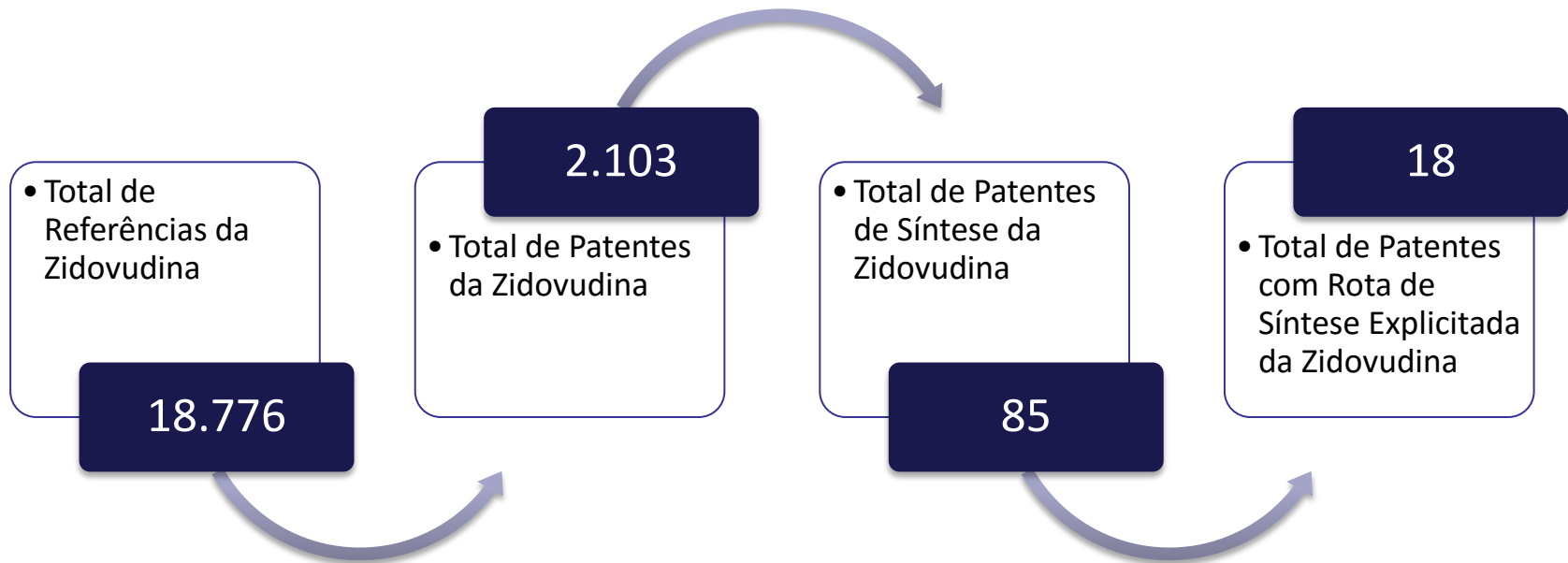
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16/09/2015

# Patentes Zidovudina





➤ [http://www.jstor.org/stable/2555803?seq=1#page\\_scan\\_tab\\_contents](http://www.jstor.org/stable/2555803?seq=1#page_scan_tab_contents)

# Patent Documents Analysis Allows

- knowledge about existing prospective industrial property rights in the country (validity, ownership, ...), particularly to avoid infringement actions;
- knowledge about the state-of-the-art in a specific technology;
- assessment of novelty and patentability of own developments with a view to applying for a domestic or foreign industrial property right;
- evaluation of a specific technology;
- identification of alternative technology and its sources;
- location of sources of know-how in a specific field in a given country;

## Patent Documents Analysis Allows (cont.)

- improvement of an existing product or process;
- development of new products or processes;
- solution of a specific technical problem;
- assessment of a particular technical approach;
- monitoring of activities of competitors both within the country and abroad;
- survey of the market in order to identify a gap or to discover new trends at an early stage

# Compares the Chemical Structures of the Zidovudine with the 14 Most Frequently Substances - STEP 5

- Recovery of structures of selected substances – SciFinder Scholar®

The screenshot displays the SciFinder Scholar web interface. The browser address bar shows the URL <https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf>. The SciFinder logo is visible in the top left, and the user is logged in as Flavia Mendes. The main navigation bar includes 'Explore', 'Saved Searches', and 'SciPlanner'. On the left, a sidebar menu lists categories: REFERENCES, SUBSTANCES, and REACTIONS. Under SUBSTANCES, 'Substance Identifier' is highlighted with a blue oval. A callout bubble labeled 'Substance Identifier' points to this menu item. The main search area, titled 'SUBSTANCES: SUBST', contains a text input field with a list of CAS numbers: 50-89-5, 29706-84-1, 104218-44-2, 4234-08-6, and 99018-98-1. A callout bubble labeled 'Substances' CAS' points to this list. Below the input field, there are examples and a 'Search' button. On the right, there are sections for 'SAVED ANSWER SETS' and 'KEEP ME POSTED'.