

# Study on the chemical composition profile of Priorix Tetra

## Introduction and description of the need

By examining the registration dossier for military vaccines, that is available in the final report <sup>1</sup> of the "Parliamentary committee of inquiry into the effects of the use of depleted uranium", <sup>2</sup> we noticed the presence of protein-chemical contaminants and impurities, thus requiring a further analytical study. Our association has decided to take charge of it, as far as possible. This project is part of such research. It has been necessary to develop a technology capable of analyzing a wide spectrum of molecules of chemical, metabolic and protein origin in order to evaluate the quality of the products obtained. A method was therefore developed, based on SANIST <sup>3-6</sup> technology to test vaccines for purity and safety (further information below).

## Results and discussion

### 1. Analysis of the composition declared in the patient information leaflet

Both batches have been analysed in order to verify the presence of the following compounds declared in the patient information leaflet: Amino acids, Lactose, Mannitol, Sorbitol, Water and Neomycin sulphate.

Such ingredients are mentioned in the datasheet as excipients and processing residuals declared by the manufacturer.

### 2. Protein fraction analysis

Peptide fragments associated with proteins probably derived from the purification process have been detected in both production batches. We have found, among others, **Sarcoplasmic calcium-binding protein** <sup>4</sup>, **Actin** <sup>5</sup> and **Vimentin**.

**Sarcoplasmic calcium-binding protein** is a recognized allergen. It can be hypothesized that injected foreign proteins could cause hypersensitivity and allergic reactions, <sup>6-7</sup> especially after vaccine recalls, but also autoimmunity due to their similarity with human proteins.

Determining the amount of these proteins is important because the greater the quantity, the more likely there could be a sensitization after vaccine recalls.

Both Actin and Vimentin are of animal origin, bovine and chicken respectively: they derive from the culture media, along with the amino acids already represented among impurities.

Name	Database	Molecular weight (KDa)	Score	Code
• Actin, cytoplasmic 1	SwissProt	42	77/50	P60712
• Sarcoplasmic calcium-binding protein	NCBI-prot	0,84	37/10	P86909.1

<sup>1</sup> <http://www.camera.it/leg17/491?idLegislatura=17&categoria=022bis&tipologiaDoc=documento&numero=023&doc=pdfel>

<sup>2</sup> [http://www.camera.it/leg17/436?shadow\\_organo\\_parlamentare=2588](http://www.camera.it/leg17/436?shadow_organo_parlamentare=2588)

<sup>3</sup> Albini A. et al., Front Endocrinol (Lausanne). 2018 Apr 5;9:110.doi:10.3389/fendo.2018.00110. (<https://www.ncbi.nlm.nih.gov/pubmed/29674995/>)

<sup>4</sup> <https://pubchem.ncbi.nlm.nih.gov/target/gene/3355102>

<sup>5</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/10008504#section=3D-Conformer>

<sup>6</sup> <https://www.hindawi.com/journals/mi/2013/261054/>

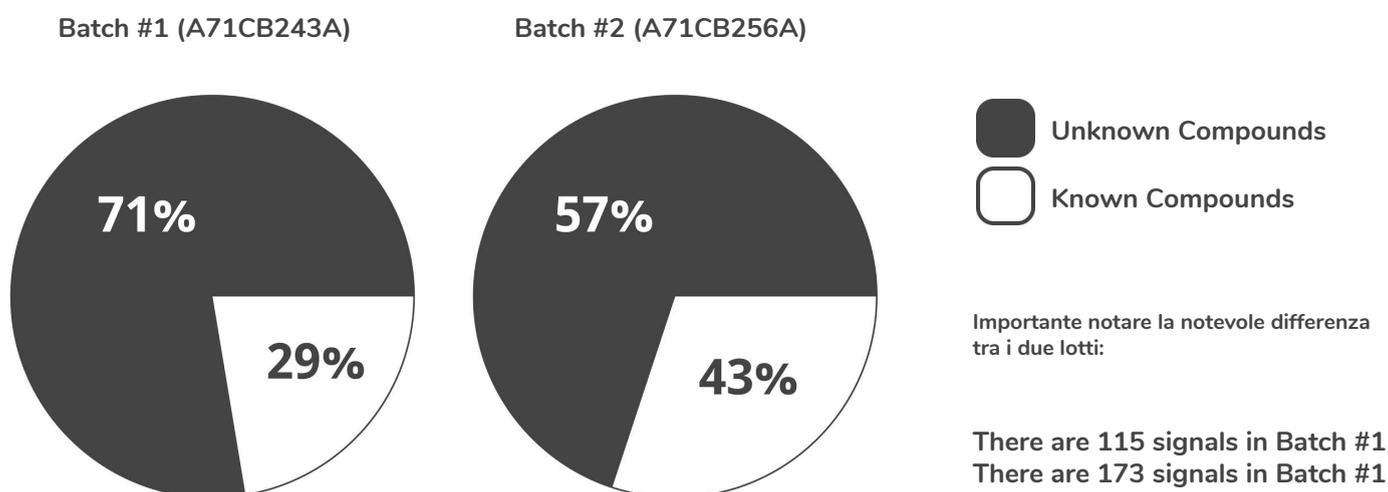
<sup>7</sup> <https://www.ncbi.nlm.nih.gov/pubmed/30009963>



### 3. Analysis of metabolic fractions

It should be noted that this screening study provides semi-quantitative data, which ranges from nanograms to micrograms as an indicative order of magnitude. It will be necessary to proceed using standard analytical certificates with a known qualification in order to obtain accurate quantitative data.

The identification screening results obtained in the two batches under examination are shown below:



**NOTES FOR UNDERSTANDING:** this is a first level analysis, that is an identification analysis based on molecular weight. If an outcome is unequivocal (i.e. a single compound is associated as a structure to a given molecular weight), it is more likely the right one, but absolute certainty is not possible in this phase. As you will notice, as far as a certain number of compounds is concerned, different substances correspond to a particular molecular weight.

#### 3.1. Priorix-Tetra Vaccine – Batch #1 (A71CB243A)

115 signals were detected, but only the 29% returned a potential classification (Table 1).

It must be specified that the identity of the compounds is not certain and must be confirmed by a second level screening carried out with certified analytical standard.

During the screening phase, instruments measure a particular data by its accurate molecular weight (measurement error <10 ppm). Then, on the basis of these measures, a molecular formula is calculated. Some formulas can correspond to several compounds having the same molecular weight but different chemical identity.



**NOTES FOR UNDERSTANDING:** in brief, the certain result is that we have found 115 chemically different substances, among which only the 29% is known.



In **Batch #1 (A71CB243A)** several chemical compounds of known structure were detected, among which\*:

Extract from Table 1

Composto	Classification
Compound <sup>8</sup>	<b>Herbicide</b> - Herbicides, also called <b>weed-killers</b> , are substances used for weed control <sup>9</sup>
Cyflumetofen <sup>10</sup>	<b>Acaricide</b> - substance capable of controlling, limiting, repelling or destroying mites, even by fighting their development <sup>11</sup>
Alkaloids	The term <b>alkaloid</b> means a naturally occurring organic compound, containing amine groups which give basic character to the structure; it has great pharmacological effects in relation to the intake of small doses of the substance <sup>12</sup>
Lincomycin Hydrochloride <sup>13</sup> , Amoxicillin or cephalosporin	<b>Antibiotics</b> are substances produced by microorganisms that can destroy other microorganisms <sup>14</sup>
3-Methyleneoxindole	Antiviral drugs are a class of chemotherapeutic agents active against infections caused by viruses <sup>15</sup>
Bacterial, human and bacterial metabolites some plants	Metabolita della morfina
1-Hydroxypyrene <sup>16</sup>	Morphine metabolite

In addition to these compounds there are also probable contaminations whose origin should be investigated in a specific way:

<b>Tamsulosin</b>	It is a selective alpha blocker used in the drug Duodart, produced by GlaxoSmithKline, for the treatment of benign prostatic hyperplasia <sup>17</sup>
<b>Sildenafil</b>	Sildenafil is used in the <b>treatment of erectile dysfunction</b> and to improve the exercise abilities in adult patients with pulmonary hypertension. Sildenafil is known by the brand name <b>Viagra, produced by Pfizer</b> <sup>18-19</sup>
<b>Gabapentin</b>	Gabapentin is the name of the active ingredient specifically indicated in postoperative pain and in partial epilepsy resistant to standard therapies. It is branded under various names, including Neurontin or Horizant <sup>20</sup>
<b>Atovaquone</b>	Atovaquone is an organic compound used as a drug in the treatment of malaria. Normally administered in combination with proguanil, a biguanide that acts against the plasmodium of malaria <sup>21</sup>

### 3.2. Priorix-Tetra Vaccine – Batch #2 (A71CB256A)

<sup>8</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/Morfamquat>

<sup>9</sup> <https://it.wikipedia.org/wiki/Diserbante>

<sup>10</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/11496052>

<sup>11</sup> <https://it.wikipedia.org/wiki/Acaricida>

<sup>12</sup> <https://it.wikipedia.org/wiki/Alcaloidi>

<sup>13</sup> [https://pubchem.ncbi.nlm.nih.gov/compound/Lincomycin\\_hydrochloride](https://pubchem.ncbi.nlm.nih.gov/compound/Lincomycin_hydrochloride)

<sup>14</sup> <https://it.wikipedia.org/wiki/Antibiotico>

<sup>15</sup> <https://it.wikipedia.org/wiki/Antivirale>

<sup>16</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/1-hydroxypyrene>

<sup>17</sup> <https://www.gsk.com/en-gb/media/press-releases/gsk-receives-european-approval-for-duodart/>

<sup>18</sup> [https://www.ema.europa.eu/documents/product-information/viagra-epar-product-information\\_it.pdf](https://www.ema.europa.eu/documents/product-information/viagra-epar-product-information_it.pdf)

<sup>19</sup> <https://www.ema.europa.eu/medicines/human/EPAR/viagra>

<sup>20</sup> <https://it.wikipedia.org/wiki/Gabapentin>

<sup>21</sup> <https://it.wikipedia.org/wiki/Atovaquone>



173 signals were detected, but only the 43% returned a potential classification (Table 2).

It must be specified that the identity of the compounds is not certain and must be confirmed by a second level screening carried out with certified analytical standard.

During the screening phase, instruments measure a particular data by its accurate molecular weight (measurement error <10 ppm). Then, on the basis of these measures, a molecular formula is calculated. Some formulas can correspond to several compounds having the same molecular weight but different chemical identity.

Extract from Table 2

Compound	Classification
Morfamquat <sup>10</sup>	<b>Herbicide</b> - Herbicides, also called <b>weed-killers</b> , are substances used for weed control <sup>11</sup>
Cyflumetofen <sup>12</sup>	<b>Acaricide</b> - substance capable of controlling, limiting, repelling or destroying mites, even by fighting their development <sup>13</sup>
Alkaloids	The term <b>alkaloid</b> means a naturally occurring organic compound, containing amine groups which give basic character to the structure; it has great pharmacological effects in relation to the intake of small doses of the substance <sup>14</sup>
Lincomycin Hydrochloride, <sup>15</sup> Amoxicillin or cefalosporin and OA-6129 E <sup>22</sup>	Antibiotics are substances produced by microorganisms that can destroy other microorganisms <sup>16</sup>
Bacterial, human and bacterial metabolites some plants	Morphine metabolite
1-Hydroxypyrene <sup>18</sup>	Human metabolite
Fluchloralin <sup>23</sup>	<b>Fluchloralin</b> has been used as a herbicide. The effect is due to the inhibition of the formation of microtubules. The active substance fluchloralin is not included in the list of plant protection products authorized in the EU. No plant protection product is authorized in Germany, Austria and Switzerland containing Fluchloralin. Its toxicity is known.

In addition to these compounds there are also probable contaminations whose origin should be investigated in a specific way:

Acetylleucyl-leucyl-norleucinal <sup>24</sup>	Tripeptide, inibitore delle proteasi
AMD 070 <sup>25</sup>	Experimental anti-HIV drug
Debrisoquin <sup>26</sup>	Member of isoquinoline alkaloids, adrenergic agent
Atovaquone	Atovaquone is an organic compound used as a drug in the treatment of malaria. Normally administered in combination with proguanil, a biguanide that acts against the plasmodium of malaria <sup>23</sup> <sup>23</sup>
Vigabatrin	Vigabatrin is an anticonvulsant drug that inhibits the catabolism of GABA, acting as Suicide substrate on GABA-transaminase, the enzyme responsible for degradation of GABA, main inhibitory neurotransmitter in humans <sup>27</sup>
Sildenafil	Sildenafil is used in the <b>treatment of erectile dysfunction</b> and to improve the exercise abilities in adult patients with pulmonary hypertension. Sildenafil is known by the brand name <b>Viagra</b> , produced by Pfizer <sup>19-20</sup>

#### 4. Final considerations

<sup>22</sup> <https://www.ncbi.nlm.nih.gov/pubmed/6547129>

<sup>23</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/fluchloralin>

<sup>24</sup> <https://chem.nlm.nih.gov/chemidplus/rn/110044-82-1>

<sup>25</sup> <https://aidsinfo.nih.gov/drugs/517/amd-070/0/patient>

<sup>26</sup> <https://pubchem.ncbi.nlm.nih.gov/compound/Debrisoquine>

<sup>27</sup> <https://it.wikipedia.org/wiki/Vigabatrin>



Significant variability in the content of contaminants and impurities appears to be present from the analyses carried out on the two batches; most of these were not characterized using the metabolic and protein reference databases (KEGG, NCBI-Prot e SwissProt).<sup>8-9</sup>  
There is a critical issue in the contamination by various compounds potentially or definitely harmful to human health.

**In summary, the first questions we asked ourselves, and the relative answers obtained, are the following:**

1. Are the chemical substances listed in the data sheet present?	Yes
2. Are there any chemical and protein contaminations?	Yes
3. How many contaminating compounds are there?	From 115 to 173
4. What are they?	Proteins, metabolites, synthetic chemical compounds

**At this point**

1. We have identified actin and vimentin as proteins
2. All the other compounds are likely as a structure
3. Each detected compound is above the nanograms as quantity

**At this point**

1. First of all it is necessary to identify with certainty at least the 9 most interesting probable compounds (see point 5)
2. Then to determine the exact quantity of each contaminant

## 5. Future development of the research

Confirmation and identity analyses will be performed using the "Tandem Mass Spectrometry (MS/MS)" technique associated with the aid of certified analytical standards. Analyses will be performed in compliance with the European directives (EU directive 2002/657 / EC) useful for the identification of compounds.<sup>29</sup>

In particular, the investigation will target the confirmation of the following substances and the evaluation of the degree of toxicity:

1. Morfamquat
2. Cyflumetofen
3. Lincomycin
4. Amoxicillin
5. Tamsulosin
6. Sildenafil
7. Gabapentin
8. Atovaquone
9. Sarcoplasmic calcium-binding protein

## 6. Description of SANIST technology



The internationally renowned SANIST platform, through publications in pre-referenced scientific journals <sup>28-29</sup>, was used to perform a first identification screening on the vaccines of interest.

## 7. Details related to the analytical method

SANIST technology consists of:

- a) a) One kit for the extraction of analytes (the unknown substances to be determined);
- b) **the LC-SACI / ESI-MS** <sup>6</sup> analysis system which allows to reduce mass spectrometers' chemical noise and obtain a better detection of instrumental signals;
- c) **the SANIST** <sup>5-6</sup> **data processing System** consisting of a local bioinformatics and network platform capable of processing data using dedicated databases and customized algorithms. It must be specified that, at screening stage, the identifying process is conducted in the field of scientific research and through research in official databases (KEGG, NCBI-Prot and SwissProt) <sup>30-31</sup> without the support of certified analytical standards. **Therefore a second level analysis with certified analytical standards is needed to be performed in order to confirm their identity.**

## 8. Fields of application of SANIST technology

Fields of application of SANIST technology:

- a. In **clinical research** of disease markers and their direct application in the diagnostic field.
- b. **Food services**, food traceability. Comparative studies to determine the products quality based on their complex molecular composition. Detection of food fraud.
- c. **Nutraceutical sector**, development of the nutritional value of a food supplement based on its molecular composition. Counterfeit search (eg: addition of drugs).
- d. **Pharmaceutical sector**, drug control and research of active biomolecules.
- e. **Cosmetic industry**: cosmetic products molecular composition can be carefully monitored and correlated with the product quality.

## 9. How to read the tables

<sup>28</sup> Albini A. et al., Rapid Commun Mass Spectrom. 2015 Oct 15;29(19):1703-10. doi: 20.1002/rcm.7270. (<https://onlinelibrary.wiley.com/doi/full/10.1002/rcm.7270>)

<sup>29</sup> Cristoni S. et al., J Mass Spectrom. 2017 Jan;52(1):16-21. doi:10.1002/jms.3895. (<https://www.ncbi.nlm.nih.gov/pubmed/27776380>)

<sup>30</sup> Kanehisa M. et al., Nucleic Acids Res. 2017 Jan 4;45(D1):D353-D361. doi:10.1093/nar/gkw1092. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5210567/>)

<sup>31</sup> Cristoni S. et al., Expert Rev Proteomics. 2004 Dec; 1(4):469-83. (<https://www.ncbi.nlm.nih.gov/pubmed/15966842>)



This is a screening phase. The instrument measures data by accurate molecular weight (measurement error <10 ppm). On the basis of these measures an empirical formula is calculated. Some formulas can correspond to several compounds having the same molecular weight but different chemical identity.

**Example of a single associated component:**

▪ Atovaquone	Drug for malaria treatment
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In this example, the instrument detected a signal with a certain molecular weight. By inserting the empirical formula in the databases, it was possible to associate a **probable component**.

**Example of a single associated component:**

<ul style="list-style-type: none"> <li>▪ Spiramine A</li> <li>▪ Butoxydim</li> </ul>	<ul style="list-style-type: none"> <li>▪ Diterpenoid</li> <li>▪ Butanone used as herbicide</li> </ul>
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In this example, the instrument detected a signal with a certain molecular weight. By inserting the brute formula in the databases, it is possible to associate **two probable components**.

## 10. Complete tables of contaminants

**Table 1 - Batch #1 (A71CB243A)**

▪ Zizybeoside I	▪ Glycoside
▪ L-Tyrosine	▪ Aa, used to prepare rotavirus vaccine (Rotarix)
▪ N-acetyl-D-fucosamine	▪ Component of the polysaccharide of some Staphilococcus Aureus strains. Vaccines based on carbohydrates.
▪ Morfamquat	▪ Bipyridine herbicide
<ul style="list-style-type: none"> <li>▪ Magnocurarine</li> <li>▪ Lotusine</li> </ul>	<ul style="list-style-type: none"> <li>▪ Member of isoquinoline</li> <li>▪ Member of isoquinoline. Alkaloid with antibacterial and antihypertensive activity</li> </ul>
▪ L-Tryptophan	▪ Amino acid
▪ L-Threonine	▪ Amino acid
▪ L-Proline	▪ Amino acid
▪ L-Phenilalanine	▪ Amino acid
▪ L-Methionine	▪ Amino acid
▪ L-Lysine	▪ Amino acid
▪ L-Leucine	▪ Amino acid
▪ Lincomycin Hydrochloride	▪ Antibiotic produced by Streptomyces lincolnensis
▪ Lichenin	▪ Glucan. Study to use glucans as vaccine adjuvants
▪ L-Histidine	▪ Amino acid
▪ L-arginine	▪ Amino acid
▪ Lactose	▪ Added as stabilizer
▪ Justicidin B	▪ Lignano
▪ Iridodial Glucoside Tetraacetate	▪ Terpene glycoside
<ul style="list-style-type: none"> <li>▪ Ethyl cinnamie</li> <li>▪ Lachnophyllum ester</li> </ul>	<ul style="list-style-type: none"> <li>▪ Cinnamic acid and ethanol Ester</li> <li>▪ Fatty Acid Ester</li> </ul>



▪ Erastin	▪ Molecule able to initiate ferroptotic cell death.
▪ D-Valine	▪ Amino acid
▪ Deethylatrazine ▪ 3-indoleacrylate	▪ Metabolite of the atrazine herbicide ▪ Monocarboxylic acid
▪ 5-Methyltetrahydrofolate	▪ Form of vitamin B (folic acid). The leukocytes produce formaldehyde starting from n5- Methyltetrahydrofolate.
▪ 5-amino-6-(phosphoribosyl)uracil ▪ phenolsulfonphthalein	▪ E. coli Metabolite ▪ pH indicator (red)
▪ 5,10-methylethilenetetrahydrofolate	▪ Formaldehyde detoxification Intermediate
▪ 3-o-ethyl ascorbic acid	▪ Vitamin C derivative
▪ 3-Methyleneoxindole	▪ Anti-viral activity against Herpes, Mengo, Poliovirus and Sindbisvirus
▪ 3-Buten-1-amine	▪ Alkylamide
▪ 2-Oxosuberate	▪ Dicarboxylic acid
▪ (R)-2-Methylpyrrolidine	▪ Pyrrolidine
▪ (4Z, 7Z, 10Z, 13Z, 16Z, 19Z)-Docosahexaenoic acid ethyl ester	▪ Polyunsaturated fatty acid
▪ THTC	▪ -
▪ Tamsulosin	▪ Active substance for urinary retention
▪ Sildenafil	▪ Cancer killer in combination with the influenza vaccine
▪ Senampeline A	▪ Alkaloid
▪ N-methyltryptamine ▪ Gramine	▪ tryptophan Alkaloid derived ▪ grasses Alkaloid
▪ Morphine-6-glucuronide	▪ Morphine metabolite. Studies on morphine-conjugated vaccines
▪ Erysotrine ▪ 3-Methoxyestra-1,3,5(10)-triene-16,17-dione 16-oxime	▪ Alkaloid ▪ Steroid
▪ Gibberellin 2-O-beta-D-glucoside	▪ -
▪ Gabapentin	▪ Epilepsy drug Active substance
▪ Dihydrochelirubine ▪ 6-oxochelirubine ▪ 7,8-Didemethyl-8-hydroxy-5-deazariboflavin	▪ Dihydrobenzophenanthridic acid alkaloid ▪ Alkaloid ▪ Riboflavin
▪ Cyflumetofen	▪ Acaricide for the control of spider mites
▪ Colchicoside	▪ Alkaloid. Acetamides Member
▪ Cassythine ▪ (6-alpha-D-glucosaminy)-1D-myo inositol	▪ Alkaloid ▪ D-glucosaminide and a monosaccharide Derived
▪ bis-D-fructose 2', 1:2, 1'-dianhydride ▪ D-Fructofuranose 1,2':2,3'-dianhydride ▪ Levofuraltadone	▪ Dianhydride sugar ▪ Dianhydride sugar ▪ An antibiotic that can be used in combination with a vaccine made up of hybrid cells for cancer treatment ▪ Heterotetracyclic compound
▪ mycrocyclosin	▪ Heterotetracyclic compound
▪ Atovaquone	▪ Drug for malaria treatment
▪ Amoxicillin ▪ Cephalexin monohydrate ▪ Cefroxadine	▪ Antibiotic ▪ Antibiotic that decreases the effectiveness of vaccines ▪ Cephalosporin Antibiotic
▪ 7-deoxyloganate ▪ 8-epideoxyloganic acid	▪ Plant metabolism ▪ Plant metabolism
▪ 4-Guanidinobutanal/ piperazine-2-carboxamide	▪ -
▪ 2-N, 6-N-Bis(2,3-dihydroxy benzoyl)-L-Lysine amide	▪ -
▪ 1-Hydroxypyrene	▪ Human Metabolite (pyrene)



▪ 17beta-hydroxy-4,17-dimethyl-4-azaandrost-5-en-3-one

▪ -

**Table 2 - Batch # 2 (A71CB256A)**

▪ Zizyboside I	▪ Glycoside
▪ Viguiestenin ▪ Picrasin G	▪ Germacranolide (plant origin) ▪ Triterpenoid
▪ Trans-cinnamate ▪ Dihydrocoumarin ▪ 4-Hydroxycinnamyl aldehyde ▪ 3-hydroxy-1-indanone ▪ 3-Isochromanone ▪ Cinnamic acid ▪ Pyruvophenone	▪ Cinnamic acid conjugate base ▪ Plant metabolism ▪ Plant metabolism ▪ - ▪ Fungal origin compound ▪ Plant origin compound ▪ Compound that is present in coffee
▪ THTC	▪ -
▪ Tamsulosin	▪ Active ingredient for urinary retention
▪ Lactose	▪ Added as stabilizer
▪ Spiramine A ▪ Butoxydim	▪ Diterpenoid ▪ Butanone used as herbicide
▪ Sildenafil	▪ Cancer killer used in combination with influenza vaccine
▪ Senampeline A	▪ Alkaloid
▪ Pradimicin B ▪ Sanggenon C ▪ Sanggenon D	▪ Pradimicine Member isolated from Actinomadura hibisca ▪ Diarileptanoid ▪ Diarileptanoid
▪ Piperidine / (R)-2-Methylpyrrolidine	▪ Plant origin compound ▪ Piyrrolidine
▪ OA-6129 E	▪ Carbapenem with antibiotic activity
▪ N-methyltryptamine ▪ Gramine ▪ Alpha-methyltryptamine	▪ Tryptophan derived Alkaloid ▪ Grasses Alkaloid ▪ Psychedelic medication
▪ Nicotyrine ▪ 1,5-Naphthylenediamine	▪ Pyridines Member ▪ Carcinogenic agent
▪ N-acetyl-D-fucosamine	▪ Component of some Staphilococcus Aureus strains polysaccharide. Vaccines based on carbohydrates
▪ Morphine-6-glucuronide	▪ Morphine metabolite. Studies on morphine-conjugated vaccines
▪ Morfamquat	▪ Bipyridine herbicide
▪ Militarinone A	▪ Fungal origin Pyridine alkaloid of
▪ Magnoshinin ▪ Eplerenone /	▪ Neolignano methoxybenzenes member ▪ Diuretic drug
▪ Estra-1,3,5(10)-triene-3,6alpha,17beta-triol triacetate ▪ Estra-1,3,5(10)-triene-3,6beta,17beta-triol triacetate	▪ Estere steroideo ▪ -
▪ L-Valine	▪ Aa
▪ L-Tyrosine	▪ Aa, used to prepare rotavirus vaccine (Rotarix)
▪ L-Tryptophan	▪ Amino acid
▪ L-Threonine	▪ Amino acid
▪ L-Proline	▪ Amino acid
▪ L-pipecolate ▪ 1-Aminocyclopentanecarboxylate ▪ N4-Acetylaminobutanal ▪ Vigabatrin	▪ L-pipecolic acid conjugate (human blood metabolite) ▪ - ▪ Urea cycle Intermediate ▪ Anti-convulsive drug
▪ L-Phenilalanine	▪ -



	<ul style="list-style-type: none"> <li>Urea cycle Intermediate</li> <li>Anti-convulsive drug</li> </ul>
<ul style="list-style-type: none"> <li>L-Methionine</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>L-Lysine</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>L-Leucine</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>Lyncomycin hydrochloride</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>Lichenin</li> </ul>	<ul style="list-style-type: none"> <li>Antibiotic</li> </ul>
<ul style="list-style-type: none"> <li>L-Histidine</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>L-Arginine</li> </ul>	<ul style="list-style-type: none"> <li>Amino acid</li> </ul>
<ul style="list-style-type: none"> <li>Justicidin B</li> </ul>	<ul style="list-style-type: none"> <li>Lignano</li> </ul>
<ul style="list-style-type: none"> <li>Isosamidin</li> <li>Peucenidin</li> <li>Pteryxin</li> <li>Samidin</li> <li>2-(4-(ethoxyphenyl)-5,6,7,8-tetramethoxy-4H-1-benzopyran-4-one</li> <li>5'-Demethylatein</li> </ul>	<ul style="list-style-type: none"> <li>Member of coumarins (plant origin)</li> <li>Furanocoumarin</li> <li>Member of coumarins (plant origin)</li> <li>Member of coumarins (plant origin)</li> <li>Tetramethoxyflavone</li> <li>Plant metabolim</li> </ul>
<ul style="list-style-type: none"> <li>Isobutyronitrile</li> <li>1-Pyrroline</li> </ul>	<ul style="list-style-type: none"> <li>Aliphatic nitrile, volatile organic compound</li> <li>Imminates cyclic</li> </ul>
<ul style="list-style-type: none"> <li>Iridodial Glucoside Tetraacetate</li> <li>8-epiiridodial glucoside tetraacetate</li> </ul>	<ul style="list-style-type: none"> <li>Terpene glycoside</li> <li>terpene glycoside</li> </ul>
<ul style="list-style-type: none"> <li>Guanine</li> </ul>	<ul style="list-style-type: none"> <li>Purine nitrogenous base</li> </ul>
<ul style="list-style-type: none"> <li>Gibberellin 2-O-beta-D-glucoside</li> </ul>	<ul style="list-style-type: none"> <li>Glycoside</li> </ul>
<ul style="list-style-type: none"> <li>Fluchloralin</li> </ul>	<ul style="list-style-type: none"> <li>Nitrocompound. Herbicide</li> </ul>
<ul style="list-style-type: none"> <li>Ethylmorphine</li> <li>¶Armepavine</li> <li>¶Erysotrine</li> <li>Laurifine</li> <li>¶6-Ethylmorphine</li> <li>3-Methoxyestra-1,3,5(10)-triene-16,17-dione 16-oxime</li> </ul>	<ul style="list-style-type: none"> <li>Opioid and antitussive analgesics</li> <li>Isokinoline</li> <li>Alkaloid</li> <li>Methoxybenzene</li> <li>Alkaloid morphine</li> <li>Steroid</li> </ul>
<ul style="list-style-type: none"> <li>Erastin</li> </ul>	<ul style="list-style-type: none"> <li>Molecule able to start ferroptosis cell death</li> </ul>
<ul style="list-style-type: none"> <li>D-ribose</li> </ul>	<ul style="list-style-type: none"> <li>Carbohydrate</li> </ul>
<ul style="list-style-type: none"> <li>Dimethylenetriurea</li> </ul>	<ul style="list-style-type: none"> <li>Condensed urae Member present in fertilizers</li> </ul>
<ul style="list-style-type: none"> <li>Dihydrochelirubine</li> <li>6-oxochelerithine</li> <li>7,8-Didemethyl-8-hydroxy-5-deazariboflavin</li> </ul>	<ul style="list-style-type: none"> <li>Dihydrobenzophenanthridic acid alkaloid</li> <li>Alkaloid</li> <li>Riboflavin</li> </ul>
<ul style="list-style-type: none"> <li>Digitalose</li> <li>D-Thevetose</li> </ul>	<ul style="list-style-type: none"> <li>Sugar</li> <li>Sugar</li> </ul>
<ul style="list-style-type: none"> <li>Deethylatrazine</li> <li>3-indoleacrylate</li> </ul>	<ul style="list-style-type: none"> <li>Metabolite of the herbicide atrazine</li> <li>Monocarboxylic acid</li> </ul>
<ul style="list-style-type: none"> <li>Debrisoquin</li> </ul>	<ul style="list-style-type: none"> <li>Isoquinoline member, adrenergic agent</li> </ul>
<ul style="list-style-type: none"> <li>Diamino-alpha-keto-dimethylphosphinothricin</li> </ul>	<ul style="list-style-type: none"> <li>-</li> </ul>
<ul style="list-style-type: none"> <li>Cyflumetofen</li> </ul>	<ul style="list-style-type: none"> <li>Acaricide spider mites the control of</li> </ul>
<ul style="list-style-type: none"> <li>Colchicoside</li> </ul>	<ul style="list-style-type: none"> <li>Alkaloid. AcetamidesMember</li> </ul>
<ul style="list-style-type: none"> <li>Cassythine</li> <li>6-alpha-D-glucosaminyll-1D-myoinositol</li> </ul>	<ul style="list-style-type: none"> <li>Alkaloid</li> <li>D-glucosaminide and a monosaccharide derived</li> </ul>



<ul style="list-style-type: none"> <li>▪ Capillanol</li> </ul>	<ul style="list-style-type: none"> <li>▪ Aliphatic alcohol</li> </ul>
<ul style="list-style-type: none"> <li>▪ Brunfelsamidine</li> <li>▪ N,N,N trimethylmethanaminium Chloride</li> </ul>	<ul style="list-style-type: none"> <li>▪ Plant origin poisonous compound</li> <li>▪ -</li> </ul>
<ul style="list-style-type: none"> <li>▪ bis-D-fructose 2', 1:2, 1'-dianhydride</li> <li>▪ D-Fructofuranose 1,2':2,3'-dianhydride</li> <li>▪ Prazepam</li> <li>▪ 2,3-Dehydro-UWM6</li> <li>▪ Levofuraltadone</li> </ul>	<ul style="list-style-type: none"> <li>▪ Dianhydride sugar</li> <li>▪ Dianhydride sugar</li> <li>▪ Benzodiazepine derivative</li> <li>▪ Phenanthrenes Member</li> <li>▪ Antibiotic that can be used in combination with a vaccine consisting of hybrid cells for cancer treatment</li> <li>▪ Heterotetracyclic compound</li> </ul>
<ul style="list-style-type: none"> <li>▪ mycrocyclosin</li> </ul>	
<ul style="list-style-type: none"> <li>▪ Barium cation</li> </ul>	<ul style="list-style-type: none"> <li>▪ Alkali metal</li> </ul>
<ul style="list-style-type: none"> <li>▪ Atovaquone</li> </ul>	<ul style="list-style-type: none"> <li>▪ Malaria treatment drug</li> </ul>
<ul style="list-style-type: none"> <li>▪ Amoxicillin</li> <li>▪ Cephalexin monohydrate</li> <li>▪ Cefroxadine</li> <li>▪ CGP 28-392</li> </ul>	<ul style="list-style-type: none"> <li>▪ Antibiotic</li> <li>▪ Antibiotic that decreases vaccines effectiveness</li> <li>▪ Cephalosporin antibiotic</li> <li>▪ Aromatic ether</li> </ul>
<ul style="list-style-type: none"> <li>▪ AMD 070</li> </ul>	<ul style="list-style-type: none"> <li>▪ Anti-HIV drug under study</li> </ul>
<ul style="list-style-type: none"> <li>▪ Acetylleucyl-leucyl-norleucinal</li> </ul>	<ul style="list-style-type: none"> <li>▪ Tripeptide, protease inhibitor</li> </ul>
<ul style="list-style-type: none"> <li>▪ 7-deoxyloganate</li> <li>▪ 8-epideoxyloganic acid</li> <li>▪ Y395153</li> <li>▪ AL-294</li> </ul>	<ul style="list-style-type: none"> <li>▪ Plant metabolism</li> <li>▪ Plant metabolism</li> <li>▪ Alkylbenzene</li> <li>▪ Plant metabolism</li> </ul>
<ul style="list-style-type: none"> <li>▪ 5-Methyltetrahydrofolate</li> </ul>	<ul style="list-style-type: none"> <li>▪ Vitamin B Form (folic acid). The leukocytes produce formaldehyde starting from n5- Methyltetrahydrofolate</li> </ul>
<ul style="list-style-type: none"> <li>▪ 5-amino-6-(phosphoribosyl)uracil</li> <li>▪ 2-caffeoylisocitrate</li> <li>▪ WIN56291</li> <li>▪ Phenolsulfonphthalein</li> <li>▪ Thiodicarb</li> </ul>	<ul style="list-style-type: none"> <li>▪ Metabolite of E. coli</li> <li>▪ Isocitric acid derivative</li> <li>▪ -</li> <li>▪ pH indicator (red)</li> <li>▪ Carbamate insecticide</li> </ul>
<ul style="list-style-type: none"> <li>▪ 5,10-methylethilenetetrahydrofolate</li> <li>▪ Minocycline</li> <li>▪ Medermycin</li> </ul>	<ul style="list-style-type: none"> <li>▪ Formaldehyde detoxification Intermediate</li> <li>▪ Antibiotic</li> <li>▪ Benzoisocromanechinone</li> </ul>
<ul style="list-style-type: none"> <li>▪ 4-Guanidinobutanol/piperazine-2-carboxamide</li> </ul>	<ul style="list-style-type: none"> <li>▪ -</li> </ul>
<ul style="list-style-type: none"> <li>▪ 4-Fluorocyclohexadiene-cis,cis-1,2-diol</li> </ul>	<ul style="list-style-type: none"> <li>▪ Hydroxyl organic compound</li> </ul>
<ul style="list-style-type: none"> <li>▪ 3-o-ethyl ascorbic acid</li> </ul>	<ul style="list-style-type: none"> <li>▪ Vitamin C derivative</li> </ul>
<ul style="list-style-type: none"> <li>▪ 3-O-(6-O-alpha-D-xylosylphospho-alpha-D-mannopyranosyl)-alpha-D-mannopyranose</li> </ul>	<ul style="list-style-type: none"> <li>▪ Xylose phosphate</li> </ul>
<ul style="list-style-type: none"> <li>3-Methyleneoxindole</li> <li>▪ Isocarbostryl</li> <li>▪ Quinolin-2-ol</li> <li>▪ 4-Hydroxyquinoline</li> <li>▪ 2(1H)-quinolinone</li> <li>▪ Indole-3-carboxaldehyde</li> <li>▪ 8-Hydroxyquinoline</li> </ul>	<ul style="list-style-type: none"> <li>▪ Oxindole Member</li> <li>▪ -</li> <li>▪ Microbial degradation Quinoline Intermediate</li> <li>▪ Monohydroxyquinoline</li> <li>▪ -</li> <li>▪ Tryptophan Metabolite synthesized by gastrointestinal bacteria</li> <li>▪ Derived from heterocyclic quinoline</li> </ul>
<ul style="list-style-type: none"> <li>▪ 3-Buten-1-amine</li> </ul>	<ul style="list-style-type: none"> <li>▪ Alkylamide</li> </ul>
<ul style="list-style-type: none"> <li>▪ 2-Oxosuberate</li> </ul>	<ul style="list-style-type: none"> <li>▪ Dicarboxylic acid</li> </ul>
<ul style="list-style-type: none"> <li>▪ 2-Naphthylamine</li> <li>▪ 1-Naphthylamine</li> </ul>	<ul style="list-style-type: none"> <li>▪ Amine naphthalene derived</li> <li>▪ Amine naphthalene derived</li> </ul>
<ul style="list-style-type: none"> <li>▪ 2-N, 6-N-Bis(2,3-dihydroxy benzoyl)-L-Lysine amide</li> </ul>	<ul style="list-style-type: none"> <li>▪ -</li> </ul>
<ul style="list-style-type: none"> <li>▪ 1-Hydroxypyrene</li> </ul>	<ul style="list-style-type: none"> <li>▪ Human metabolite (pyrene)</li> </ul>



