ÚKZÚZ

CENTRAL INSTITUTE FOR SUPERVISING AND TESTING IN AGRICULTURE

NATIONAL REFERENCE LABORATORY

Department of Testing Plant Protection Product

Work carried out in the Czech Republic

(version for CIPAC website)

Olga Nováková

CIPAC Symposium 24th June 2014, Liege, Belgium

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REORGANIZATION
OF FORMER STATE PHYTOSANITARY ADMINISTRATION (SPA)

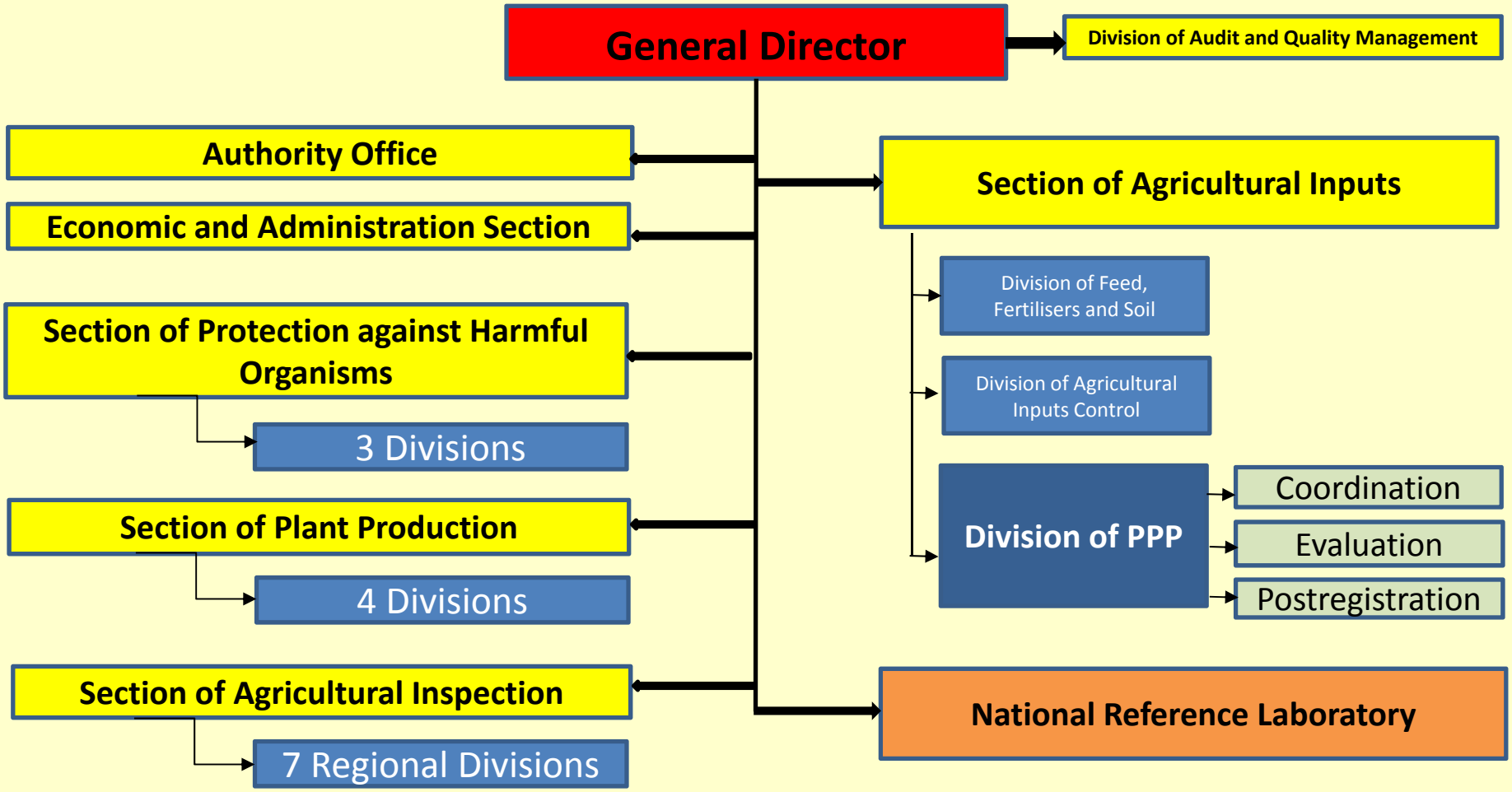
1997-2013: 2 institutes

- **SPA (State Phytosanitary Administration)**
  - Postregistration Control Division
    - **Department of Laboratory Testing Pesticide (= NRL for PPP)**
- **CISTA (Central Institute for Supervising and Testing in Agriculture)**
  - Division: National Reference Laboratory (9 laboratories)

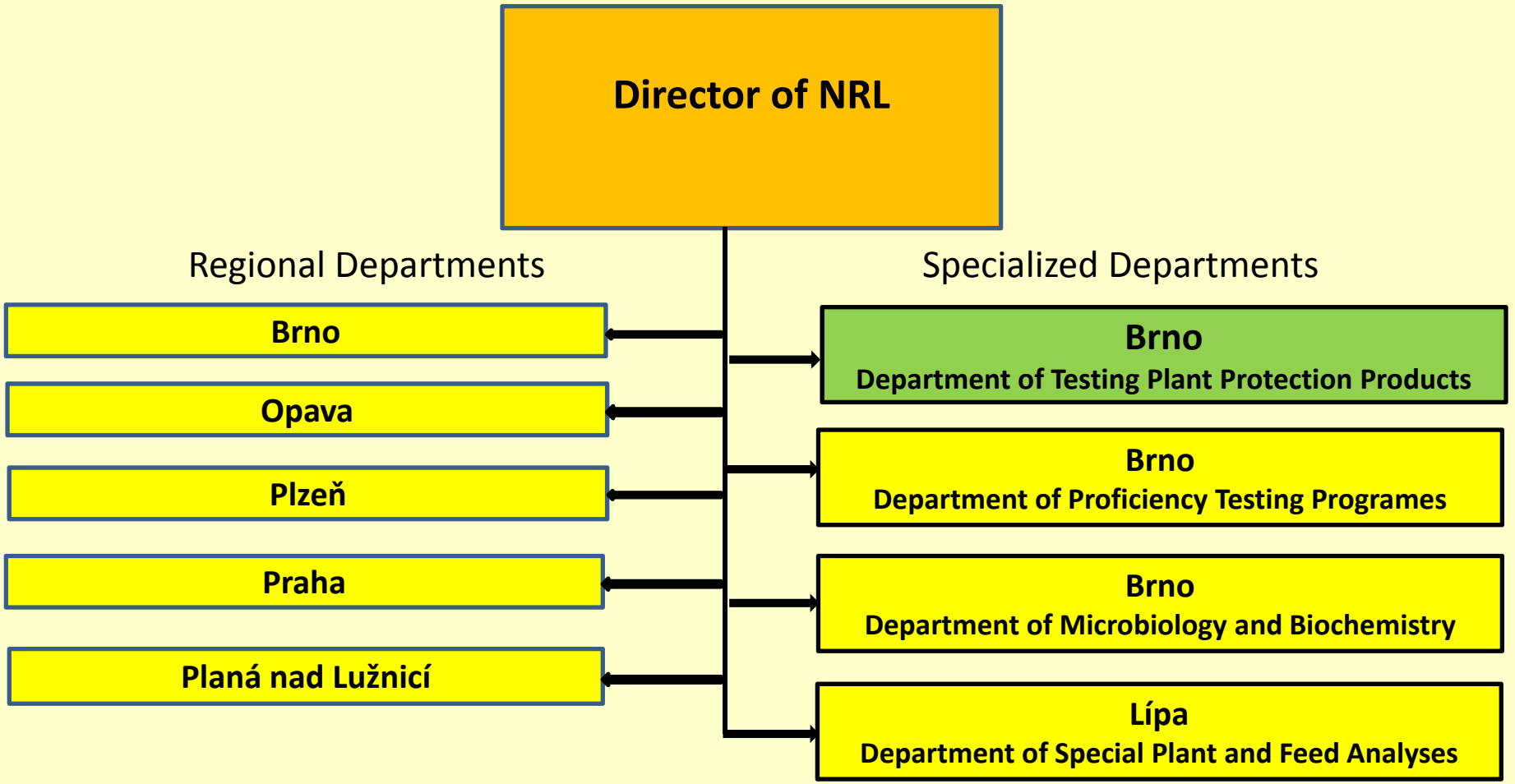
From 1.1.2014: 1 institute

- **SPA + CISTA = CISTA**
  - Division: National Reference Laboratory (9+1 laboratories)
    - **Department of Testing Plant Protection Products =** former Laboratory Testing Pesticide

STRUCTURE OF CENTRAL INSTITUTE FOR SUPERVISING AND TESTING IN AGRICULTURE (CISTA)



STRUCTURE
OF NATIONAL REFERENCE LABORATORY



DEPARTMENT OF TESTING PLANT PROTECTION PRODUCTS

Head of Department

Laboratory of chromatographic methods

Laboratory of physicochemical methods

Czech Accreditation Institute
Public Service Company
110 00 Praha 1 – Nové Město, Opletalova 41
issues this

CERTIFICATE OF ACCREDITATION

No. **210 / 2008**

to

Testing Laboratory No. **1521**

State Phytosanitary Administration
Laboratory of Pesticides
Zemědělská 1a, 613 00 Brno

Scope of accreditation:

Physical, chemical and technical tests of plant protection products to the extent as specified in the appendix to this Certificate which is attached.

Ing. Olga Nováková shall act on behalf of the accredited testing laboratory, and Ing. Olga Nováková, Ing. Jindřich Foltýn and Ing. Jiří Pryček shall be responsible for the correctness of relevant test reports.

This Certificate of Accreditation was issued by the Czech Accreditation Institute, Public Service Company, on the basis of assessment of fulfilment of the accreditation criteria in accordance with

ČSN EN ISO/IEC 17025:2005

and after having found that the testing laboratory had been qualified for objective and independent testing to the extent of the scope of accreditation.

In its activities, performed within the scope and for the period of validity of this Certificate, the holder of this Certificate is entitled to use the identification "Accredited Testing Laboratory No. 1521" next to its name provided it observes all relevant regulations relating to the activity of accredited testing laboratory including regulations issued by the Czech Accreditation Institute, Public Service Company.

Should it be proved that the holder of this Certificate fails to meet the accreditation criteria decisive for the issue hereof and the obligations conditioning accreditation, the Czech Accreditation Institute, Public Service Company, may either suspend the validity of or withdraw or change this Certificate.

This Certificate is valid until: **14 May 2011**

Prague: 23 May 2008

Jiří Růžička
Director
Czech Accreditation Institute
Public Service Company

Instruction:
The holder can enter a written objection against this Certificate, provided it concerns the scope of accreditation, in 10 days from the receipt hereof. Timely submitted objection has no dilatory effect.

SYSTEM OF POSTREGISTRATION CONTROL – responsibility

Sampling
original packages

Post-registration Control Department - responsibility

- annual plan with cooperation of laboratory
- sampling original packages - PPP samples are taken directly in the distributor stores
- labeling control
- control of sale, storage and use of PPP
- control of technical state of application machinery

Laboratory analysis
+
report

Laboratory- responsibility and competence

- **Laboratory analysis**
- laboratory check on physical and chemical properties of plant protection products and other plant protection preparations and chemical compositions
- report of analysis (+results with evaluation)

Evaluation
of results in accord with act

Post-registration Control Department – responsibility

- reconvey the rest of samples
- evaluation of results from laboratory in accord with act (law)
- information of authorization holders
- fine

LABORATORY CONTROL OF PPPs

Planned samples

- postregistration control according to annual plan
- samples within the process of PPP approval

Unplanned samples

- unknown samples
- suspicious samples (e.g. counterfeit)

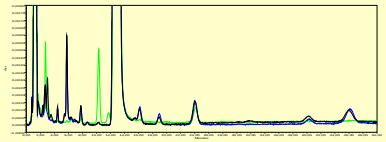
Proficiencies tests (AAPCO, AFSCA, …)

STEPS OF LABORATORY CONTROL

- Registration of samples (LIMS)
- Laboratory sampling
  - Original sample package is higher 1L or 1kg
  - Original sample package is lower 1L or 1kg

  Partition of laboratory sample = Analytical sample

- Laboratory analysis
- Evaluation of laboratory analysis
  - Certificate of analysis (Agreement or disagreement with specification)
  - Detailed expert reports



LABORATORY ANALYSIS

Planned samples – postregistration control according to annual plan

FAO specification or existing national specification

- Identity and content of active substances
- Identity and content of relevant impurities
- Physical, chemical and technical properties
- Storage stability tests

Xylene in EC formulations

Samples from parallel import – chromatographic and FTIR comparison with reference sample.

Methods: CIPAC, OECD or equivalent and the validated methods of producers, which are submitted as part of registration dossiers.

Laboratory verifies all methods according to standard operation procedure (SOP-PP-08-01).

LABORATORY ANALYSIS – cont.

Samples within the process of PPP approval

Aim:

- Verify input data (technical specification)
- Verification or validation analytical methods in CZ conditions (different column…)
- Obtain knowledge of PPP
- Focus on chemical composition
- Time for discussion of laboratory analysis -analytical results with authorization holders
- Input data for postregistration control
- Future - Help with detection of counterfeit

LABORATORY ANALYSIS – cont.

Unplanned control PPPs samples

- Unknown samples (samples without label, confusion of active ingredient,…)
- Suspicious samples

LABORATORY ANALYSIS – SUSPICIOUS SAMPLES

- Identity and content of active ingredient
- Identity and content of relevant impurities
- Physical, chemical and technical properties
- Chemical composition of sample (co-formulants, impurities,…)
- Comparison with reference sample (GC, LC, FTIR)

Additional tests for clarification of unregistered sample:

GC/MS, FTIR, Particle size distribution (CIPAC MT187), Determination of Sulphated ash (CIPAC MT29), Pour and tap bulk density (USP2/ASTM), Density, Viscosity (CIPAC MT192), Surface tension (OECD 115), TGA method, DSC method

EXAMPLES OF ANALYSIS

Appearance:

Differences of shape granules between reference sample and suspicious sample

Differences in colour between reference sample and suspicious sample

EXAMPLES OF ANALYSIS

Density:

	Density [g/ml]
Reference PPP	1,170
Suspicious PPP	**1,126**

Result:

Suspicious PPP is probably diluted or has different chemical composition.

EXAMPLES OF ANALYSIS

Density:

	Density [g/ml]	Dean – Stark (CIPAC MT 30.2) Amount of water (% w/w)	Amount of active ingredient (%)
Reference PPP	1,170	44,6	30,4
Suspicious PPP	**1,126**	**60,7**	**21,8**

Confirmation:

- **determination of water by Dean-Stark (CIPAC MT 30.2)**
- **determination of amount active ingredients**

Result:

Suspicious sample is diluted.

EXAMPLES OF ANALYSIS

Sulphated ash (CIPAC MT 29):

Reference PPP (different batches)	
year	Sulphated ash [% w/w]
2001	1,52
2003	1,30
2006	1,37
2008	1,22
2012	1,26
2013	1,05
average	**1,29**

Suspicious PPP	
Year	Sulphated ash [% w/w]
2001	---
2003	**15,52**
2006	---
2008	**19,40**
2012	**10,52**
2013	**8,62**
2013	**6,83**

Result:
There are difference between inorganic ions in suspicious sample and reference sample - the chemical composition of suspicion sample is different from reference sample.

EXAMPLES OF ANALYSIS

Surface tension (OECD 115):

PPP	Surface tension of 0,01% w/w solution (mN/m)	Surface tension of 0,5% w/w solution (mN/m)	Surface tension of 1,0 % w/w solution (mN/m)
Reference PPP	57,0	32,9	32,7
Suspicious PPP	59,4	**69,9**	**71,8**

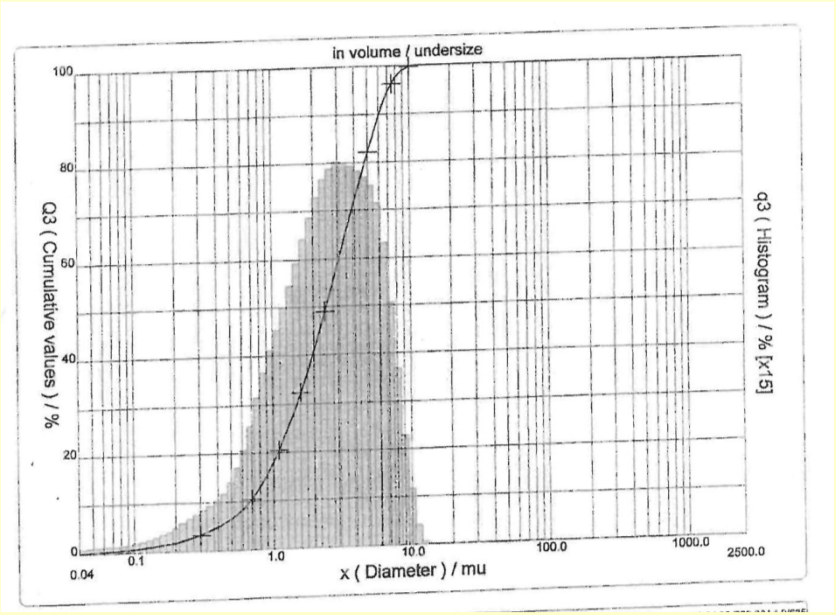
Result:

Suspicious PPP probably does not contain surface active agent.

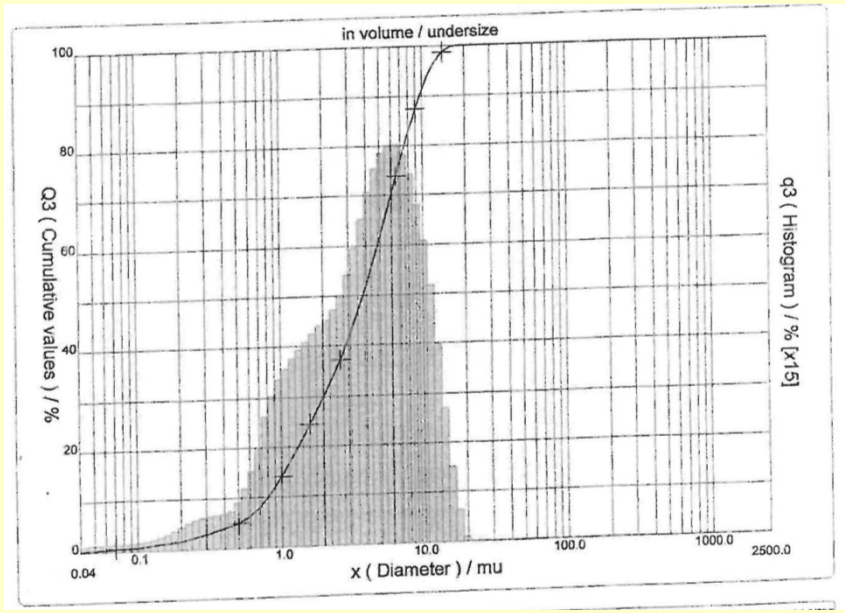
EXAMPLES OF ANALYSIS

Particle size distribution (CIPAC MT 187) :

Reference PPP



Suspicious PPP



EXAMPLES OF ANALYSIS

Particle size distribution (CIPAC MT 187) :

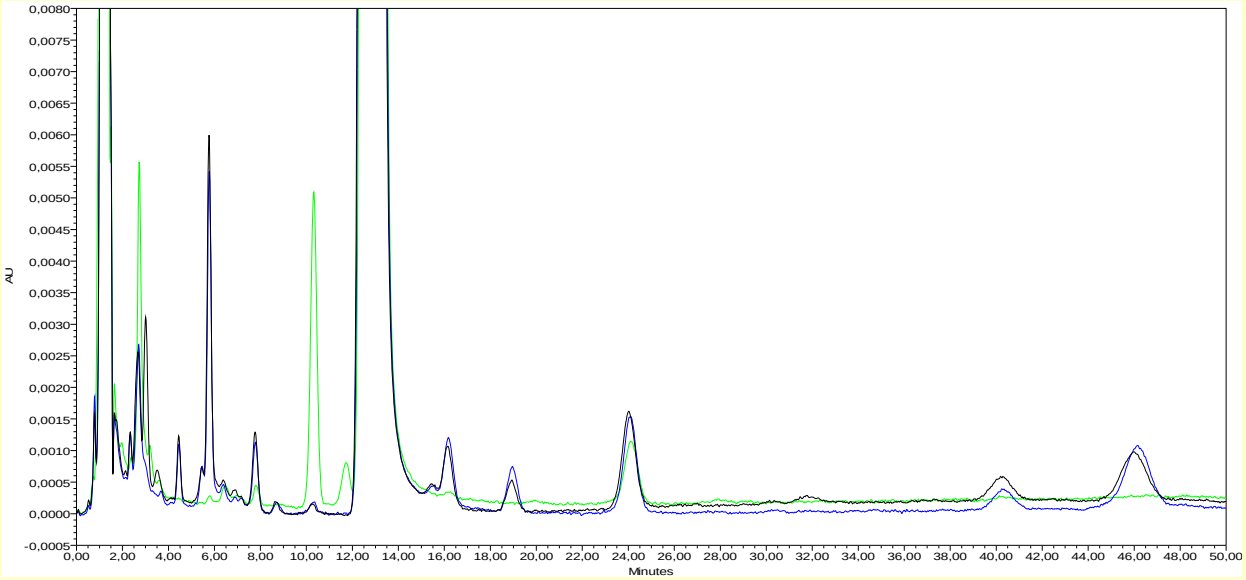
	Reference PPP	Suspicious PPP
Diameter at 10%	0,68 µm	**0,80 µm**
Diameter at 50%	2,45 µm	**3,77 µm**
Diameter at 90%	6,07 µm	**9,68 µm**
Mean diameter	2,97 µm	**4,56 µm**

Result:

Particle size distribution of particles which disperse in water in suspicious PPP are different.
It means that it can be different technology of production.

EXAMPLES OF ANALYSIS

HPLC screening by HPLC/UV:



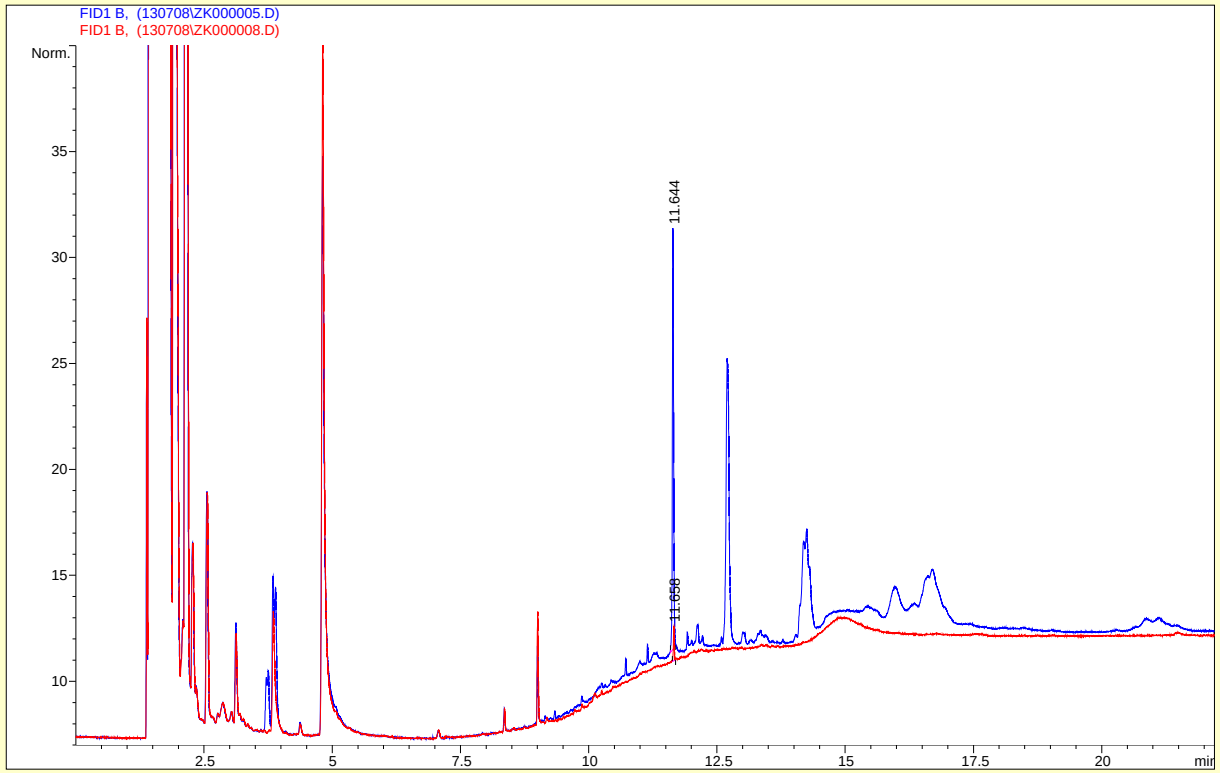
Reference PPP (black),
Suspicious PPP 1 (blue)
Suspicious PPP 2 (green)

Result:

Suspicious PPP 1 has probably identical chemical composition with reference PPP,
Suspicious PPP 2 has not identical chemical composition with reference PPP.

EXAMPLES OF ANALYSIS

GC/FID – identification of co-formulant:

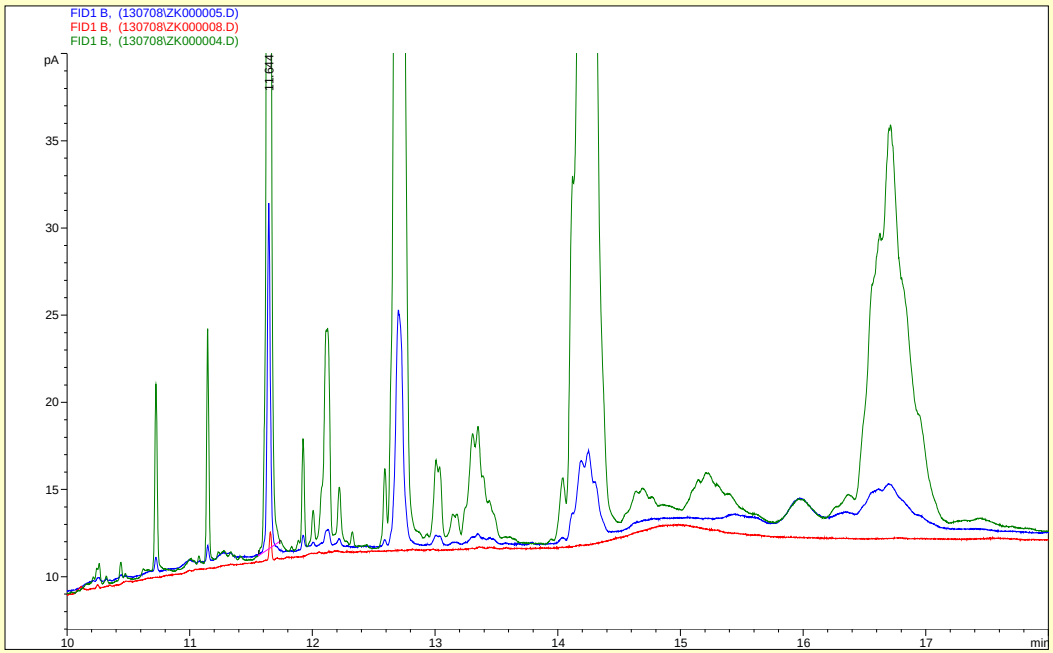


Reference PPP (blue)
Suspicious PPP (red)

EXAMPLES OF ANALYSIS

GC/FID – identification of co-formulant:

Overlay chromatograms of reference PPP and suspicious PPP and Surface-active agent, extract 10-18min



Reference PPP (blue)
Suspicious PPP (red)
Surface-activ agent (green)

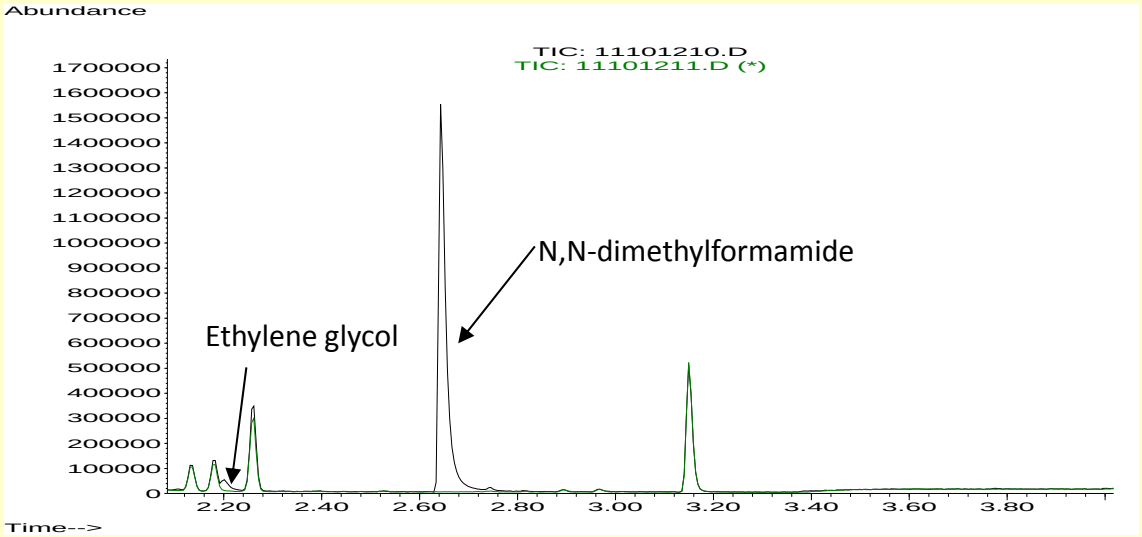
Result:

Suspicious PPP does not contain surface-active agent which is present in reference PPP.

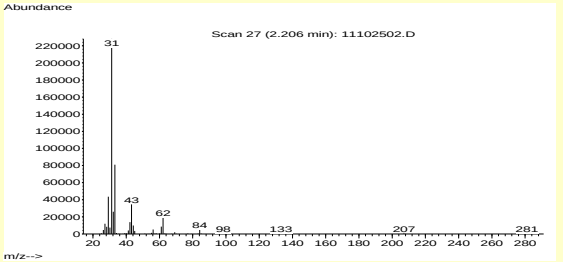
EXAMPLES OF ANALYSIS

GC/MSD identification of co-formulants:

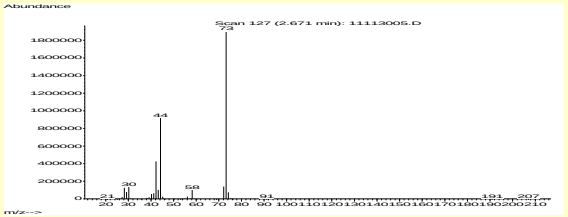
GC/MSD chromatographic profile of PPP (split 100:1, extract 2-4min)



MSD spectrum of ethylene glycol



MSD spectrum of N,N-dimethylformamid

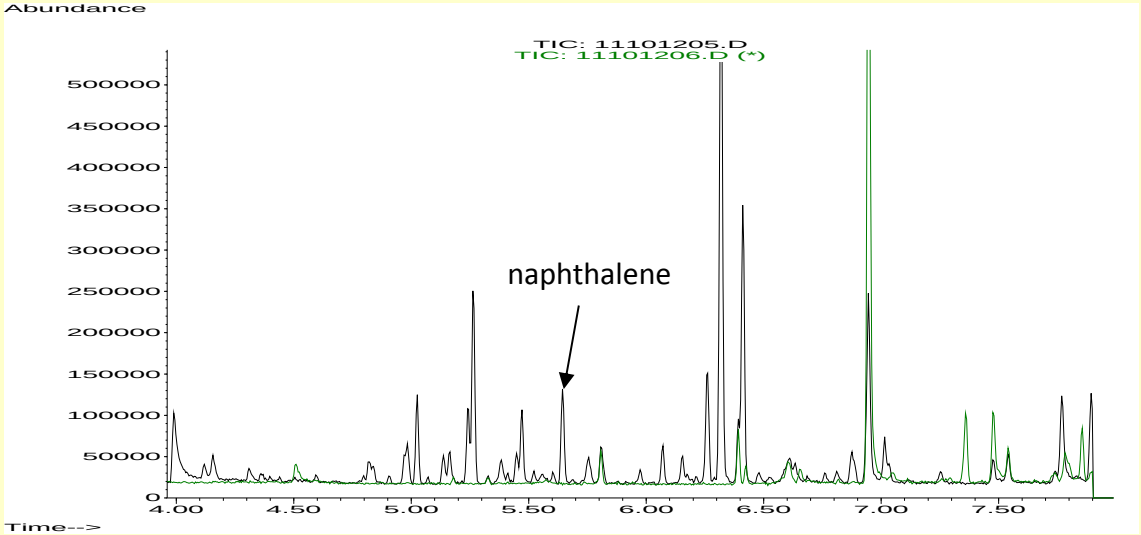


Reference PPP (green), Suspicious PPP (black)

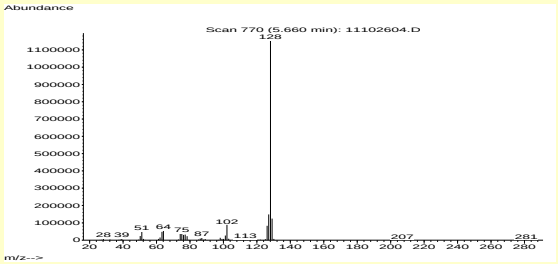
EXAMPLES OF ANALYSIS

GC/MSD identification of co-formulants:

GC/MSD chromatographic profile of PPP (split 10:1, extract 4-8min)



MSD spectrum of naphthalene

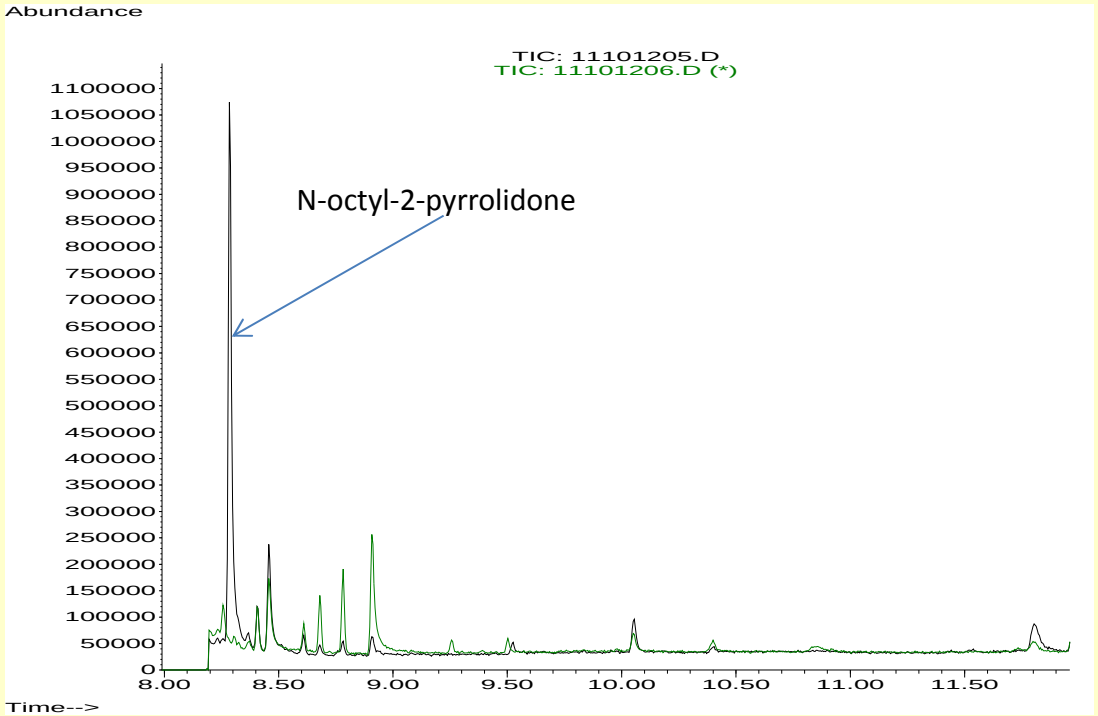


Reference PPP (green), Suspicious PPP (black)

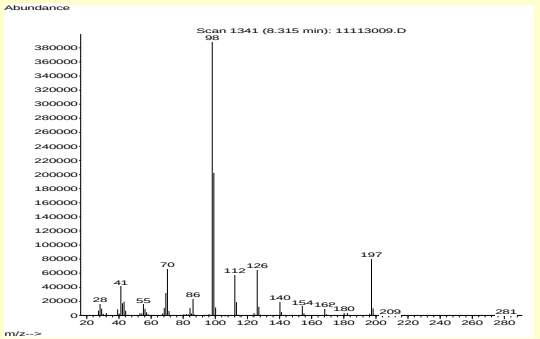
EXAMPLES OF ANALYSIS

GC/MSD identification of co-formulants:

GC/MSD chromatographic profile of PPP (split 10:1,extract 8-11,6 min)



MSD spectrum of N-octyl-2-pyrrolidone

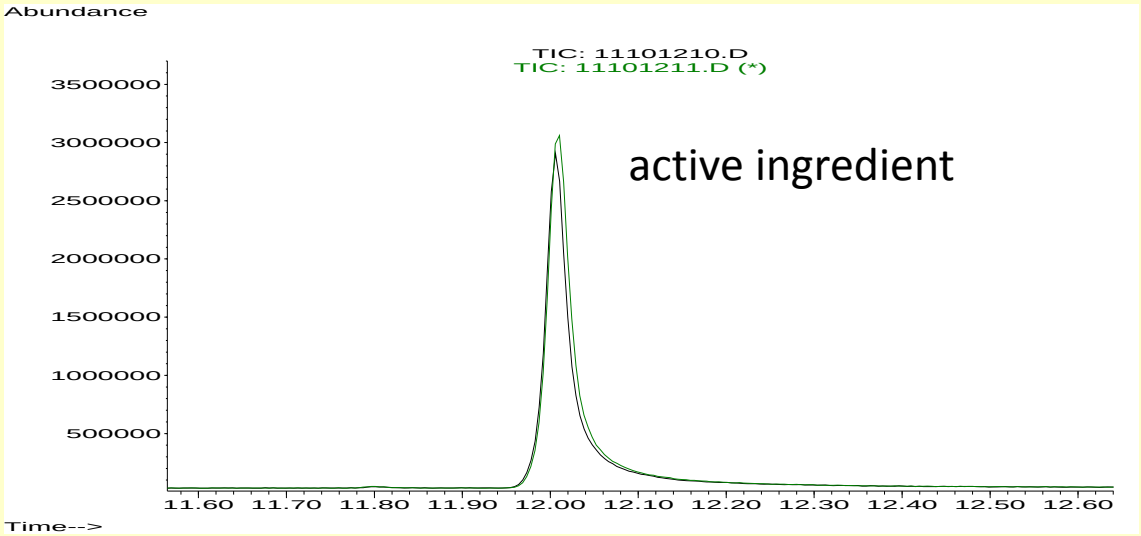


Reference PPP (green), Suspicious PPP (black)

EXAMPLES OF ANALYSIS

GC/MSD identification of co-formulants:

GC/MSD chromatographic profile of EW formulation PPP - active ingredient (extract 11,6-12,6 min)



Reference PPP (green), Suspicious PPP (black)

EXAMPLES OF ANALYSIS

GC/MSD identification of co-formulants:

Summary:

Identified components	Reference PPP	Suspicious PPP	Content % w/w
N,N-dimethylformamide	No	**Yes**	**16,78**
N-octyl-2-pyrrolidone	No	**Yes**	**0,306**
Ethylene glycol	No	**Yes**	**1,525**
Naphthalene	No	**Yes**	**0,018**

Result:

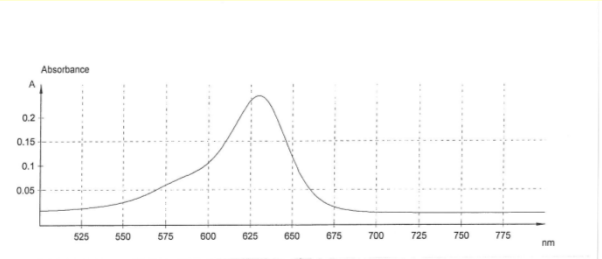
The chemical composition of suspicious PPP are different from reference sample.

EXAMPLES OF ANALYSIS

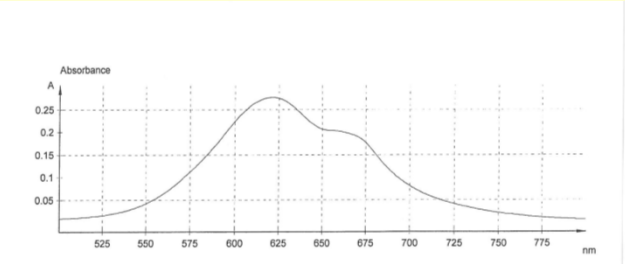
UV-VIS spectroscopy:

VIS spectrum:

Reference PPP



Suspicious PPP



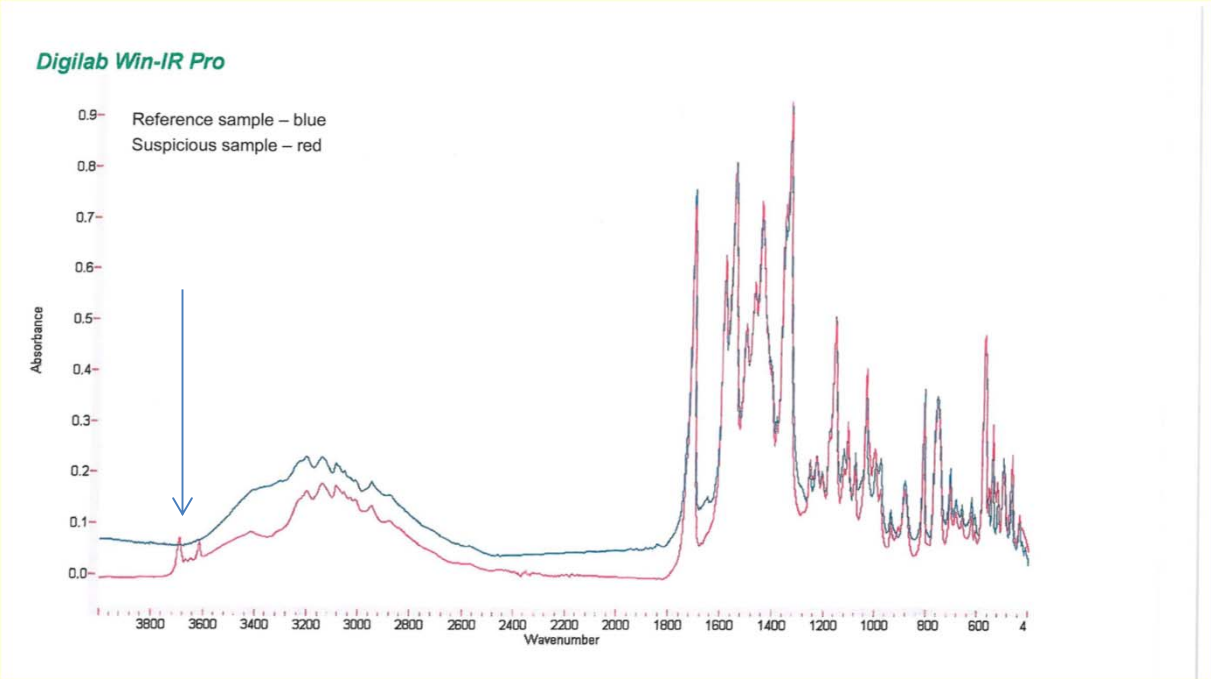
Sample	λ max v DI water [nm]
Reference sample	628 nm
Suspicious sample	**620 and 657 nm**

Result:

The suspicious PPP does not contain the same dye as reference sample.

EXAMPLES OF ANALYSIS

FTIR spectroscopy :

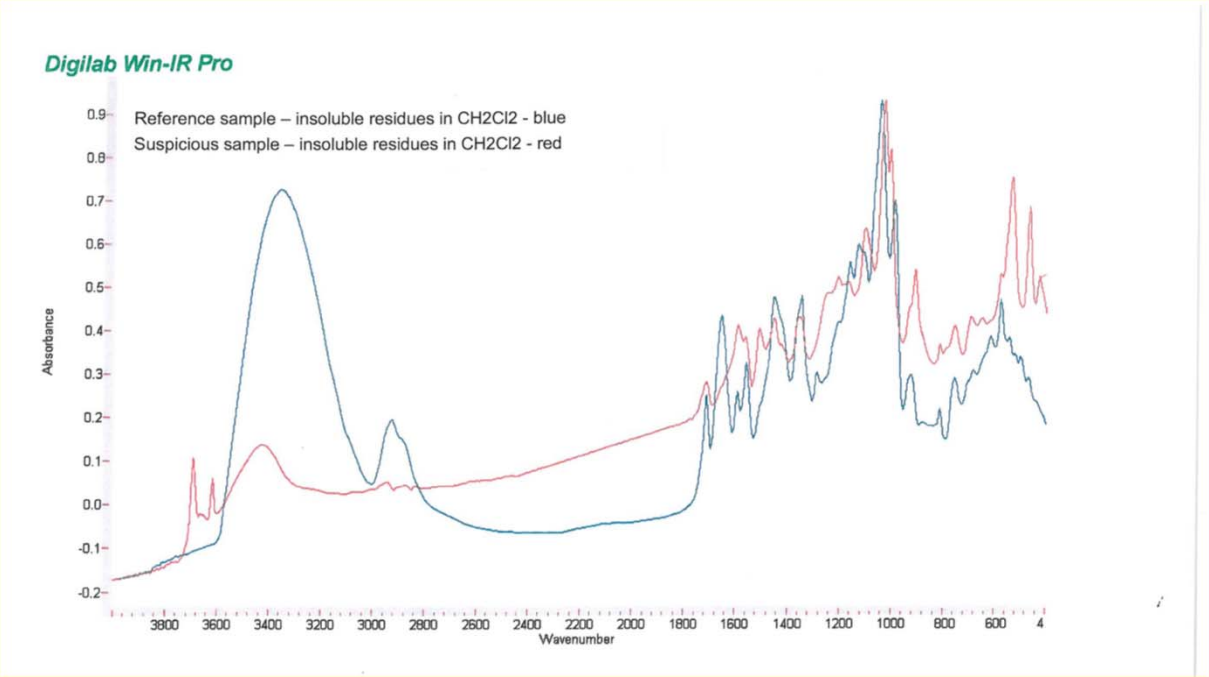


Reference PPP (blue),
Suspicious PPP (red)

EXAMPLES OF ANALYSIS

FTIR spectroscopy :

FTIR spectrum of Insoluble residues of PPP in CH_2Cl_2

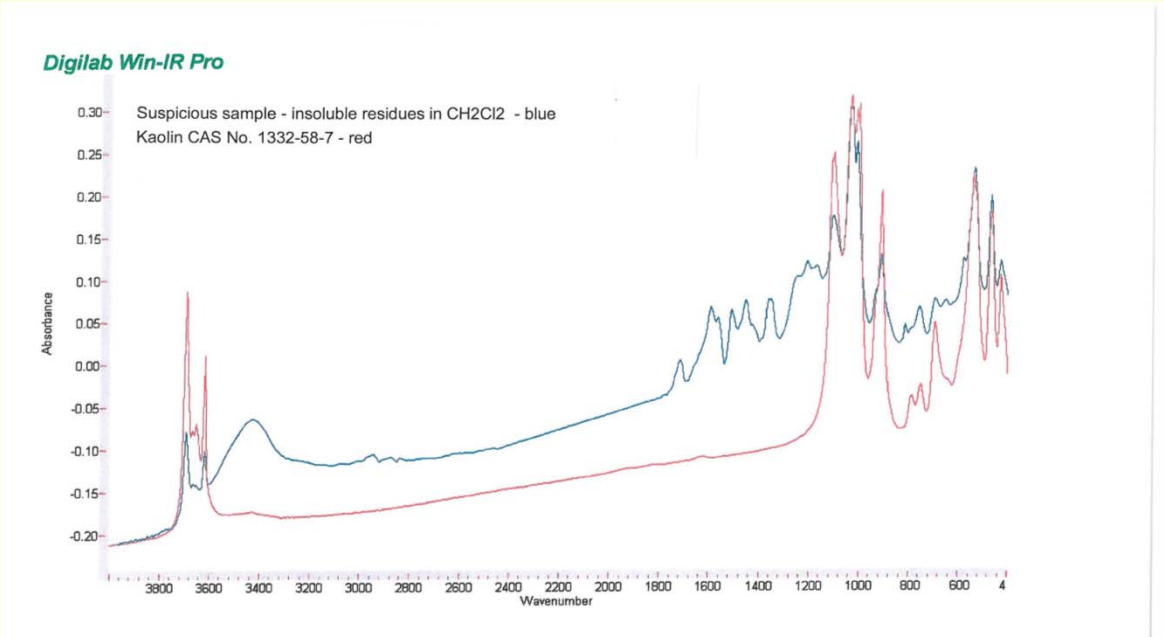


Reference PPP (blue),
Suspicious PPP (red)

EXAMPLES OF ANALYSIS

FTIR spectroscopy :

FTIR spectrum of Insoluble residues of suspicious PPP in CH_2Cl_2 and kaolin CAS No. 1332-58-7



Suspicious PPP (blue),
kaolin CAS No. 1332-58-7(red)

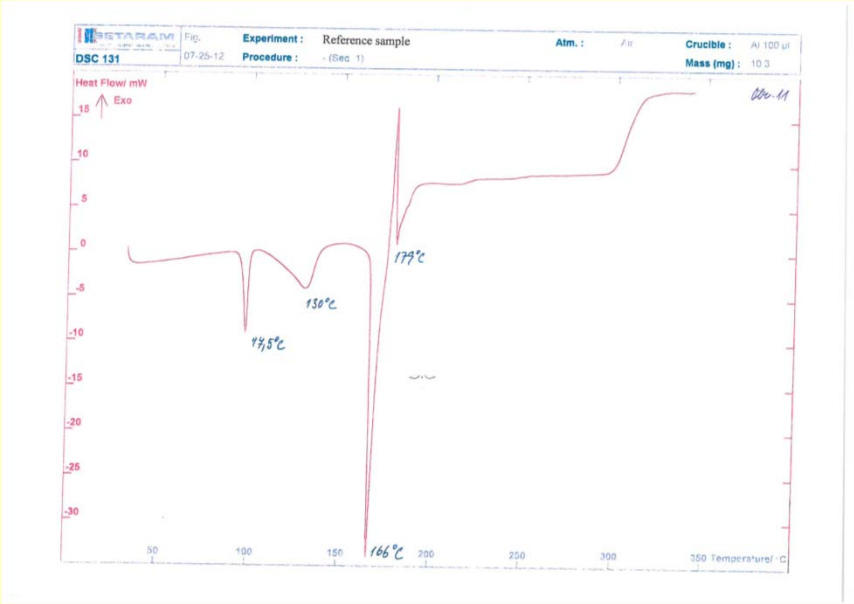
Result:

The suspicious PPP contains kaolin = the chemical composition is different from reference sample.

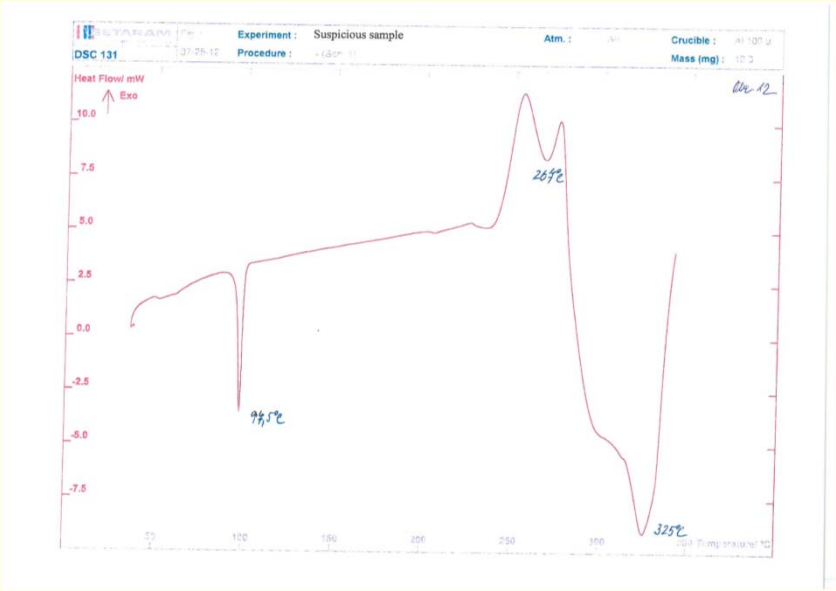
EXAMPLES OF ANALYSIS

Differential Scanning Calorimetry (DSC):

Reference PPP



Suspicious PPP



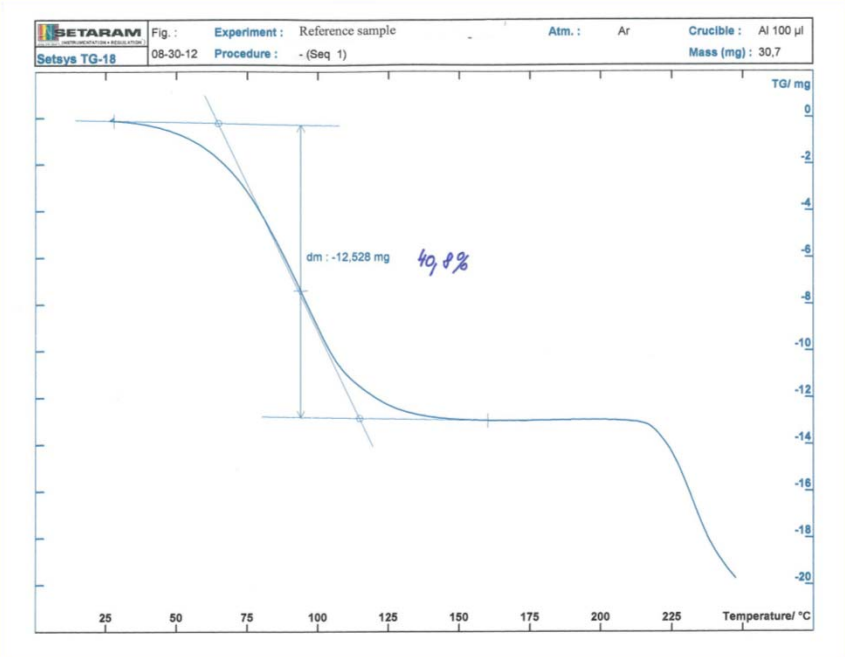
Result:

The chemical composition of suspicious sample is different from reference sample.

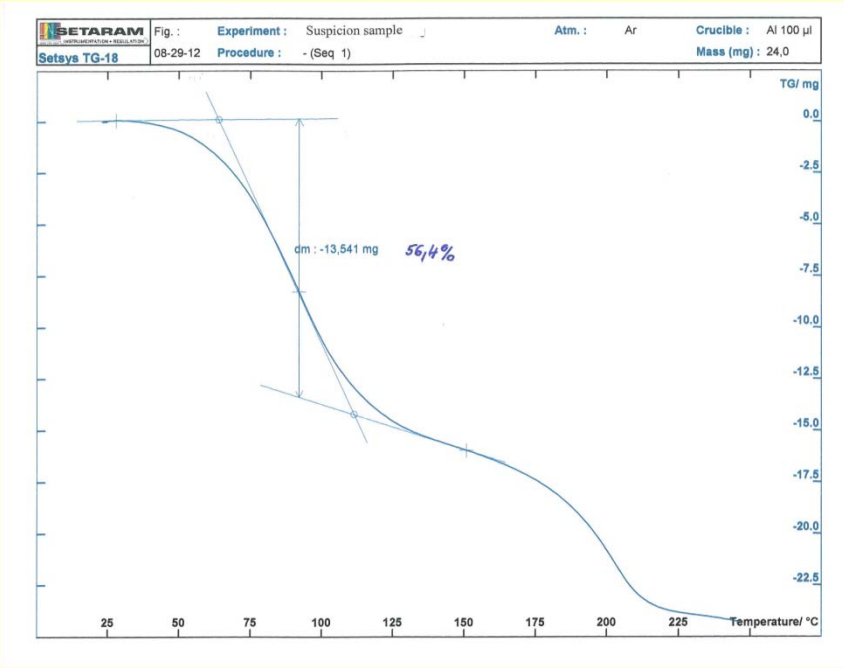
EXAMPLES OF ANALYSIS

Thermogravimetric analysis (TGA):

Reference PPP



Suspicious PPP



Result:

Different chemical composition of volatile compounds present in PPP or/and other compounds in PPP.

CONCLUSION

- Active ingredients and relevant impurities in suspicious PPP mostly agree with specification.
- We usually find differences in chromatography profile and/or in FTIR spectra between reference and suspicious samples:
  - we use the other technics and methods for identification.
- Necessity of cooperation between laboratories of national authority and producers (in interpretation of raw data, support of analytical method, standards…)
- Necessity of clear legislation.

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CENTRAL INSTITUTE FOR SUPERVISING AND TESTING IN AGRICULTURE

NATIONAL REFERENCE LABORATORY

Department of Testing Plant Protection Product

THANK YOU FOR THE ATTENTION!

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