Analytical strategies for formulation analysis

of plant protection products obtained during official market control

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Contents

- Background: Working group formulation laboratories
- Differentiation according to sample type
- **Analytical strategies**
- Analytical methods

Background

EU Working group formulation laboratories

- During a BTSF workshop in 2015 a need for cooperation and information/knowledge sharing between laboratories carrying out formulation analysis of plant protection products (ppps) was identified
- Thus a EU working group of formulation laboratories was established
- One laboratory representative per member state
- Annual meetings starting from autumn 2016

Background

EU Working group formulation laboratories

- During a first exchange of experiences and current approaches it was found that the way formulation analysis is conducted varies considerably between member states
- Analyses conducted depend on laboratory's background, institutional background and available equipment
- This may mean different levels of effectiveness regarding control of ppps on the market
- Repeated criticism during HFAA (Health and Food Audits and Analysis, formerly FVO) audits that scope of formulation analysis is not broad enough

Background

EU Working group formulation laboratories

- As a priority work item the working group established the development of guidelines for analytical strategies and interpretation of results
- Two sub-groups were formed for the two topics
- Drafts of the guidelines were presented at the meeting of the whole working group in September 2017, where it was decided to combine and harmonise the two documents as several areas of overlap ocurred
- The draft of a joint document has recently been circulated to member states for commenting

Guideline on analytical strategies

Aims of the guidance document

- EU legislation mandates official controls (Art. 68 of Regulation 1107/2009) but says nothing about the scope of formulation analysis; this gap should be closed
- A harmonised approach on how to perform formulation analysis should be established
- A baseline level of analysis for all laboratories should be established (minimum scope)
- In the medium term this should result in a more effective and efficient formulation analysis of ppps sampled during official market control

Guideline on analytical strategies

General idea

- The guideline should constitute a "cookbook" for the procedures to be followed in formulation analysis
- It should contain "recipes" for different sample types
- It should contain a ranking of the relevance of various analytical techniques
- Deviations from general workflows are possible but need to be justified
- Specific circumstances need to be taken into account – "use your brain"!

Sample types

Different analytical strategies

- Different workflows for different sample types

- **Definition of sample types**
  - Routine samples vs. suspicion samples
  - Reference samples
  - Original products: authorisation according to Art. 28
  - Parallel trade products: permit according to Art. 52 based on identity with a ppp already authorised in the member state of introduction (reference product)

Sample types

Different analytical strategies

- **Routine samples**
  - Original products or parallel trade products
  - No prior indication of non-compliance
  - Non-targeted analysis to check compliance with authorisation

- **Suspicious samples**
  - Original products or parallel trade products
  - Taken as part of an investigation based on a certain incident that raised suspicion (e.g. complaint, prior non-compliance, suspicious appearance)
  - Targeted analysis to ascertain whether the suspicion of non-compliance can be confirmed
  - Followed by further analysis, if required, to check other aspects for compliance with authorisation

Analytical strategies

Requirements

- To be able to perform formulation analysis along the lines of the analytical strategies laboratories must have the required resources:
  - Sufficient staff
  - Specialised equipment for physical-chemical tests
  - Possession or access to chromatographs and mass spectrometers, especially GC-MS
  - *Alternative*: outsourcing of certain analyses in labs of other member states

- Laboratories must have access to (confidential) full composition of the plant protection product

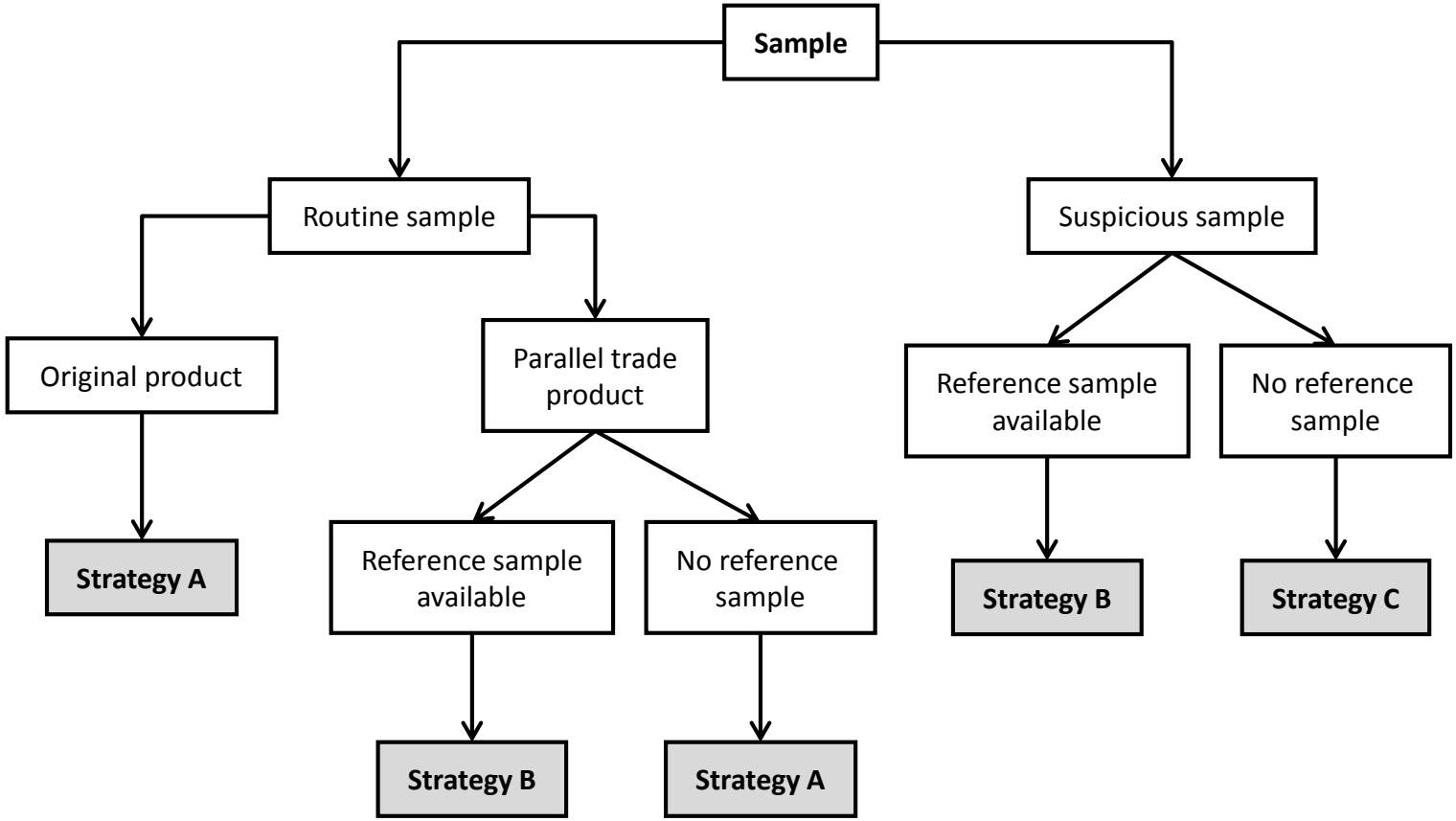
Analytical strategies

General approach

- Analytical strategies should be followed step by step (performance of several steps in parallel may be applicable)
- Mandatory and optional steps
- Additional methods not mentioned may of course be performed if the laboratory sees them to be useful
- As soon as a non-compliance is determined unequivocally the workflow should be quit
- **Overall idea: Use analytical ressources in the most effective and efficient way possible!**

Analytical strategies

Selection according to sample situation



Analytical strategies

Strategy A: Routine samples without reference ppp

- Three mandatory steps:
  1.) Appearance
  2.) Active substance identity and content
  3.) GC-MS screening *or* physical-chemical properties
  (depending on the composition of the ppp)

- Three optional steps:
  4.) Physical, chemical and technical properties
  (if not already analysed)
  5.) Co-formulants identity and content
  6.) Relevant impurities identity and content
  (possibly include in step 2 if many samples with the same active substance)

Analytical strategies

Strategy B: Sample with reference ppp

- Four mandatory steps:
  1.) Appearance
  2.) Profiling by GC-MS, FTIR spectroscopy, GC-FID, LC-UV, LC-MS, etc. (comparison of ppp "fingerprints")
  3.) Physical, chemical and technical properties
  4.) Active substance identity and content

- Two optional steps:
  5.) Co-formulants identity and content
  6.) Relevant impurities identity and content

- *Caution!* The reference sample may not necessarily comply with its authorisation and thus its validity needs to be checked

Analytical strategies

Strategy C: Suspicious sample without reference ppp

- Four mandatory steps:
  1.) Appearance
  2.) GC-MS screening
  (if the composition of the ppp suggests that GC-MS screening will not be useful this step should be skipped)
  3.) Active substance identity and content
  4.) Physical-chemical properties

- Two optional steps:
  5.) Co-formulants identity and content
  6.) Relevant impurities identity and content

Analytical methods

Information on various analyses

- Following the analytical strategies the guideline provides some hints and remarks concerning the methods used therein
- No detailled method descriptions are given instead reference to literature (e.g. CIPAC methods)
- Multi-methods seen as useful, especially if samples contain many different active substances / co-formulants
- GC-MS screening as especially powerful tool
- Methods for physical, chemical and technical properties may sometimes be troublesome but can be an easier alternative to chemical analysis

Analytical methods

The power and challenge of GC-MS screening

- Methodology:
  - All volatile compounds of the ppp that are extracted into a certain organic solvent are analysed by GC-MS in full-scan mode
  - Library search for the mass spectra of the chromatographic peaks
  - (Tentatively) identified compounds are compared with the composition of the ppp, considering chemical/technological knowledge

- **Additional, changed or missing compounds can be identified**

- Possibly further confirmation and quantification of additional compounds ("foreign substances")

- Can be quite tedious but provides a lot of information on many samples

Analytical methods

Physical, chemical and technical properties

- From the wide range of methods for testing physical, chemical and technical properties a selection was made based on the following factors:
  - uniform criteria exist for the evaluation of compliance across different formulation types (FAO/WHO manual)
  - method should provide information on certain co-formulants that are difficult to analyse otherwise

- A table contains the methods to be performed for a certain formulation type with a ranking from 1 to max. 5 (of which max. 3 are mandatory tests)

THANK YOU

for your attention!