# SECTION 3
# "FIT FOR PURPOSE APPROACH"

Welcome to third and final lesson of module 1. During this presentation, I will talk about the parameters you need to consider to chose an adequate method of analysis. In a broader way, other part of the procedure like sampling and sample prep will be introduced.

## RISK ANALYSIS

Needs for analytical measures

- Risk assessment
  - presence in food of dietary significance for the contaminant;
  - presence in food that are widely consumed;
  - food intake data for average and most exposed/high consumer groups;
  - data on intake by susceptible groups;
- Monitoring
- Quality control
- Research and development

135 - Deltamethrin

Functional class: **Insecticide**

| Commodity | MRL | Year of Adoption |
|---|---|---|
| Apple | 0.2 mg/kg | 2004 |
| Carrot | 0.02 mg/kg | 2004 |
| Cereal grains | 2 mg/kg | 2004 |
| Citrus fruits | 0.02 mg/kg | 2004 |
| Eggs | 0.02 mg/kg | 2004 |
| Flowerhead brassicas (includes Broccoli: Broccoli, Chinese and cauliflower) | 0.1 mg/kg | 2004 |
| Fruiting vegetables, cucurbits | 0.2 mg/kg | |
| Grapes | 0.2 mg/kg | 2004 |
| Hazelnuts | 0.02 mg/kg | 2004 |
| Kidney of cattle, goats, pigs and sheep | 0.03 mg/kg | 2004 |
| Leafy vegetables | 2 mg/kg | 2006 |
| Leek | 0.2 mg/kg | 2004 |
| Legume vegetables | 0.2 mg/kg | 2004 |



From a regulatory perspective, food products have to be tested to certify they are safe, but they also have to be analysed to verify their compliance with food regulations. Just a reminder that government regulations are not the only ones, as private regulations co-exist like for voluntary certifications for example. However, food analysis is also a important cornerstone of risk analysis. Typically, a part of the risk assessment relies on data obtained thanks to analyses.

Other good reasons to analyse a product are quality control and research and development. To compete in the marketplace, food companies must produce foods that meet consumer demands, comply with government regulations, and meet quality standards of the company. Reasons to analyse food products can be diverse. As this training is about food contaminants, the focus will be put on those compounds but food products could be tested for many many things (Labelling, nutrition, vitamins, etc.). In some cases, the cost of goods is linked directly to the composition as determined by analytical tests. For example, in the dairy field, butterfat content of bulk tank raw milk determines how much money the milk producer is paid for the milk.

This demonstrate the need for robust and accurate analytical methods in the domain of food science in general

## FIT FOR PURPOSE APPROACH

Module 1 - lesson 3 53

Numerous methods are often available to assay food samples for a specific food contaminant. However, there is a need to differentiate a method and a technique. By definition, a method is the application of a technique for a specific analyte in a specific matrix. So, on the screen, you can see equipment for LC- and GC-MS which are both techniques, but can be used for the development of methods for the quantification of pesticides in barley, for example.

A procedure explaining how to apply a method to a particular sample, including information on obtaining samples, handling interferents, and validating results, are needed in order to reach quality requirements. In the same way, a protocol, which is a set of guidelines specifying a procedure that must be followed have to be create if an agency is to accept the results. Protocols are common when the result of an analysis supports or defines public policy.

Using a “fit for purpose” approach relies on the assessment of method performance to define the suitability of a given methodology to provide an answer to a given requirement. To select methods used to determine or quantify food contaminants in foodstuffs, one must used analytical methods that fit their intended purpose. A fit for purpose approach includes several components like the analysis of the compounds of course, but also the sampling, the sample preparation and the treatment of the results.

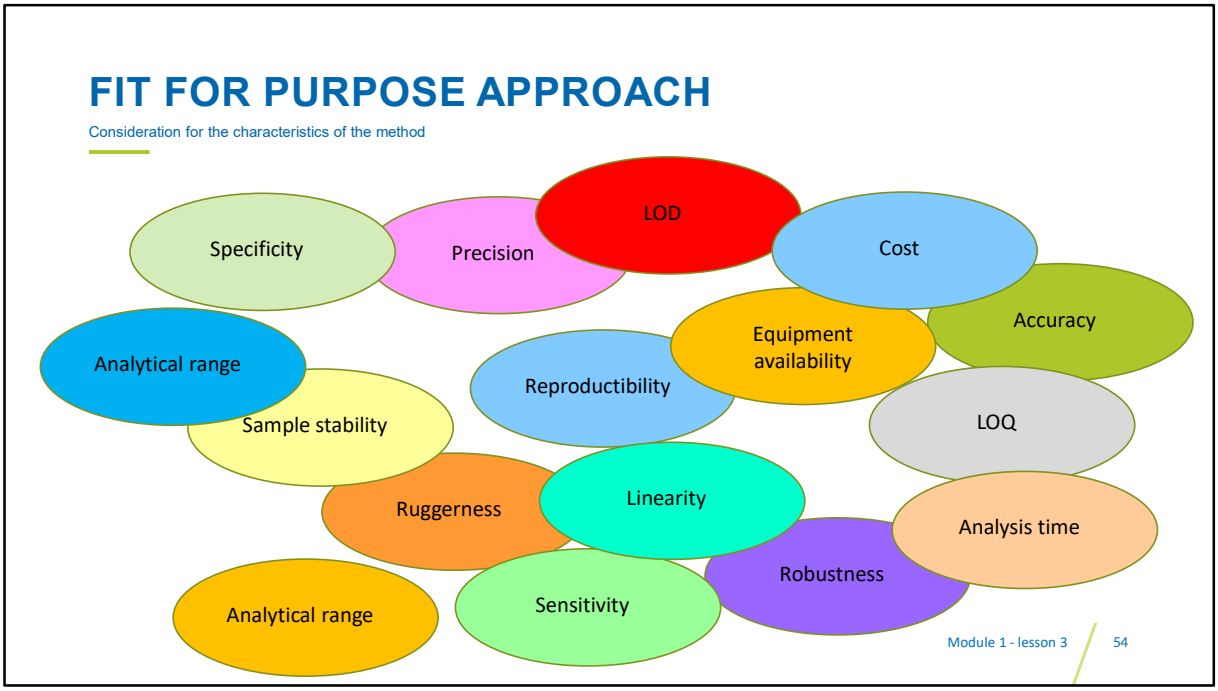
In order to analyse a sample, the first question is always: does an analytical method exist? Or do you have to develop it? As explained in lesson 2, there is not point to regulate a food contaminant if you cannot detect it. Consequently, if there is a regulatory requirement for a specific food contaminant, there is or there are methods that exist to detect or quantify the food contaminat in question.

Several nonprofit scientific organizations have compiled and published these methods of analysis for food products, which have been carefully developed and standardized. They allow the comparison of results between different laboratories that follow the same procedure, and for evaluating results obtained using new or more rapid procedures.

Among those nonprofit organizations, the AOAC international provides a lot of methods for almost all food contaminants that were presented in lesson 1 and for a large range of food products. The official methods developed are intended for use by regulated industries, regulatory agencies, contract research organizations and testing laboratories, and academic institutions. AOAC International also has programs to develop standards, to test the performance of commercial and analytical methods, and for testing laboratory proficiencies.

However, AOAC is not the only organisation providing methods, others like ISO or AFNOR also published methods for food analysis. In addition there are several organizations specialized in certain foodstuffs providing methods for a limited number of matrices. Nevertheless, when several options are available for analysis, you have to make a choice.

It is important that data generated from food monitoring yields acceptable trueness and precision for use in complex risk assessment calculations and statistical analyses. In the same way, regulators who enforce maximum residue levels (MRLs) must have confidence that the reported analytical results represent the true residue concentrations. In quality assurance and research activities, a precise estimate of the true contaminant concentration of a lot becomes important and the absence of a well-designed sampling plan will result in the collection of unrepresentative samples which will invalidate the results of subsequent contaminant determination.




The requirements of the analysis will determine the best method. According to the Codex guidelines, official methods of analysis elaborated by international organizations occupying themselves with a food or group of foods should be preferred.

To chose a method, preference should be given to methods of analysis of which the reliability have been established in respect of several criteria.

As you can see on the screen, these criteria includes among others :
Accuracy, Sensitivity, Selectivity, Robustness, Ruggedness, Precision, repeatability intra-laboratory (within laboratory), reproducibility inter-laboratory (within laboratory and between laboratories) and many others
All of these criteria have been described extensively in the scientific literature.

All analytical methods provide some variability in the results. It is important that methodology is chosen so this variability does not impinge on whether it can answer the question that is responsible for the measurement. For example, if a methodology is very susceptible to minor changes in temperature or timing it will probably not be practical in a production or field testing environment. However, the same methodology could be perfectly acceptable in a temperature controlled laboratory with highly trained technicians.

All analytical measurements have a range of analyte that they accurate for. It is important to chose a method that ensures that the value of the analyte of interest falls within this range. Measuring analytes outside of this range can lead to erroneous results. For example if the analyte is present below the limit of detection or, on the contrary, it is so high that it gives inaccurate or variable results.

Importantly, it not always necessary to chase zero. If all that is important is the knowledge that a food contaminant is present below a certain value (or not present above a certain level) then it is not always necessary to quantitate it below that value. That is why you do not always need the absolute best analytical method, but rather the one that achieves the wanted goal. It is always possible to find a better, more accurate methodology for the measurement of a food contaminant, with very few exceptions.

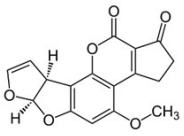
However, the following questions have to be answered before the start of any analysis:

- Can the method be carried out in a timely manner?
- Does the cost of doing the method or the equipment involved prohibit the use of the method?
- Can it be done in a reliable way by the staff available?

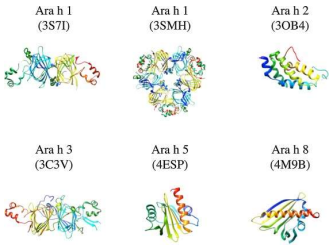
## FIT FOR PURPOSE APPROACH

Consideration for the contaminant

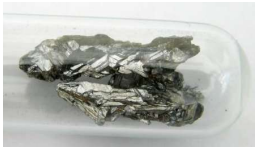
- Type of contaminants



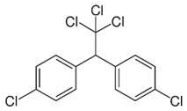
Aflotoxin B1
(1 coumarine and 3 furans)




Peanut allergens (proteins)



Arsenic



DDT



Several considerations regarding the contaminant can dictate the choice of technique for analysis

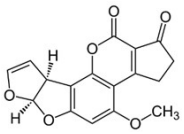
For aflatoxin, for example, you may use a lateral flow device, an ELISA test, or a LC-MS method among others.
For the detection of peanut allergens, you may use a lateral flow device or an ELISA. You might also use LC-MS method even if methods for the quantification of food allergens are still not practical.
For heavy metals, like arsenic, the options are quite limited. ICP-MS is the most used technique so far and probably the best fit for this kind of contaminants.
For pesticides like DDT, the best options are LC or GC-MS even there are some ELISA kits that can be used for the detection of a one singular pesticide.

However, for official methods, this type of consideration should have been cleaned before the publication of the method.

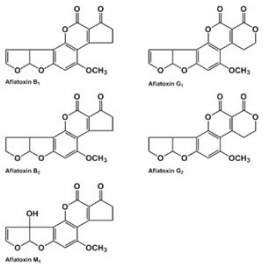
## FIT FOR PURPOSE APPROACH

Consideration for the contaminant

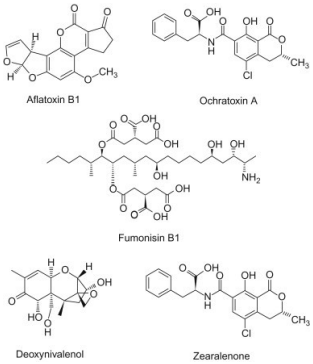
- Definition of the food contaminant we are looking for?



Aflotoxin B1



Aflotoxins




Mycotoxins



Another very important question is what is the definition of what you are looking for.

This may be looks like a silly question but it is in fact a key point.
You have to remember that regulatory requirements may be different from a food product to another. So what is called mycotoxins in wheat or barley may include mycotoxins that are not considered in other cereals. Consequently the choice of the analytical method could be different.

When you have to detect mycotoxins, does it mean all mycotoxins? Or a subgroup of mycotoxins like aflatoxins? Or even a specific mycotoxin of this subgroup?

The answer to this question will impact your choice of methodology. If you need to detect only one mycotoxin, I would suggest to choose an ELISA method but if you want to detect 10 different mycotoxins, a better fit would be a LC-MS method.

## FIT FOR PURPOSE APPROACH

Consideration for the food matrice

- What type of food matrix?
  - Impact on the results
  - Impact on the sample preparation
  - Impact on the sampling

Module 1 - lesson 3 57

Another key point is that the selected method should be chosen such that it is unaffected by other components in the sample. This is important as it ensures that the result is an accurate reflection of the question being asked. For example, there are potential inhibitors in certain food matrices regarding ELISA test leading to false positive or negative results. In the same way, some interferents can lead to inaccurate results in LC or GC methods.

Another extremely important point is the sample preparation that could be completely different from a food matrix to another.
A good example is the method for pesticides detection which provides sample preparation for all the different types of food based on their composition in water and lipidic contents. As you may imagine, the detection of pesticides in hops or meat needs different extraction protocols for the two food products. In the same way, water samples may only need a light extraction process.

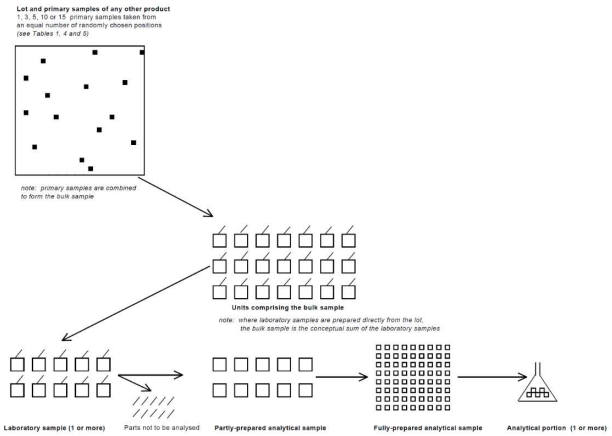
Methods for preanalytical sample preparation of foods should accomplish one or all of the following functions:

- separate target molecules from the food,
- increase their concentration,

- purify them from extraneous material,
- achieve volume reduction in bulk samples,
- produce a homogeneous sample, and
- exclude inhibitory substances.

Unfortunately, food matrices are often a tough challenge, which limits many novel method applications. Foods cover a large variety of commodities, so a universal preparative method is virtually impossible to develop. Despite best efforts to prepare the matrix for detection, residual, food-associated compounds frequently interfere with the detection assay. This is probably where

## SAMPLING PLAN




Module 1 - lesson 3 58

Finally, another key element of a fit for purpose approach is the sampling and the sampling plan. It is important that data generated from food monitoring yields acceptable trueness and precision for use in complex risk assessment calculations and statistical analyses. In the same way, regulators who enforce maximum residue levels must have confidence that the reported analytical results represent the true residue concentrations. In quality assurance and research activities, a precise estimate of the true contaminant concentration of a lot becomes important and the absence of a well-designed sampling plan will result in the collection of unrepresentative samples which will invalidate the results of subsequent contaminant determination.

A sampling plan is defined by a test procedure and a defined accept/reject limit. A test procedure is a multi-stage process and generally consists of three steps: sampling, sample preparation, and quantification (or analysis). The sampling step specifies how the sample

will be selected or taken from the primary sample to the analytical sample. Regulatory agencies, including the Codex Alimentarius, wrote some guidelines to perform sampling for the determination of contaminants in food and feed. In fact, the figure on the slide came from the Codex guidelines and represents a generic sampling plan. The European Union (EU) has also established sampling plans for a variety of commodities in accordance with the Codex guidelines.

In the end, the measured contaminants concentrations in the sample are used to estimate the food contaminants concentration in the bulk lot or compared to a defined accept/reject limit that is usually equal to a legal limit. Because of the uncertainty associated with a sampling plan, the true food contaminant concentration of a bulk lot cannot be determined with 100 % certainty; nor can all lots be correctly classified into good and bad categories with 100 % accuracy.


We have reach the end of the first module. It was really design to increase your background about food contaminants of how food regulations are developed.
The following modules will focus mostly on the different methods used to detect and quantify food contaminants starting with ELISA.

Do not forget to complete the self evaluation document before the beginning of the second module.