

# Proposed Regulatory Framework for Pesticide Residues in Food

Workshop on Pesticide Residue Testing

## **Analytical Performance Criteria Approach in Pesticide Residues Analysis**



6 May 2011



# Trend of Method Development (1)

- ❖ Number of pesticides used is continuously increasing worldwide
- ❖ In order to fulfil the needs of speeding up analytical time and improving the **quality**, the direction of method development has also been changed :
  - Traditionally, international organizations and different national / regional institutions would publish **standards** or **reference test methods** for specific pesticides





# Trend of Method Development (2)

- Regarding the test method recognition and quality control, the international trend has gradually changed:
- developing prescribed test methods
  - ➔ establishment of analytical performance criteria
- satisfactory comparability of results can be achieved by employing different analytical methods but with performance meeting the same requirements under internationally recognised protocols





# Trend of Method Development (3)

- ❖ Different laboratories can use relevant criteria protocols or reference methods compiled by international or national organizations, or adopt appropriate test methods and fulfil the quality requirements being specified according to their:
  - testing needs & intended purposes
  - facilities & resources



# Key Elements on Method Performance

- Accuracy / Trueness
- Precision
- Specificity & selectivity
- Limit of Detection (LOD)
- Limit of Quantitation (LOQ)
- ↳ Reporting limit



# Current Status

Comprehensive international and national guidelines on the requirements of analytical methods and validation protocols :

- **Codex**
- **EU**
- **OECD**
- **IUPAC**
- **HKAS (HKSAR, China)**
- **AQSIQ (P. R. China)**
- **etc.**





# Examples of General Guidelines

| ORGANIZATION         | DOCUMENT REFERENCE                                | TITLE   |
|----------------------|---|---|
| Codex                | CAC/GL 40-1993,<br>Rev. 2003, Amend. 2010.        | Guidelines on Good Laboratory Practice in Pesticide Residue Analysis                              |
|                      | ---   | Codex Alimentarius Commission Procedural Manual, 19 <sup>th</sup> Edition                         |
| EU                   | SANCO/10684/2009                                  | Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed |
|                      | Commission Decision 2002/657/EC, Annex            | Performance Criteria, Other Requirements and Procedures for Analytical Methods                    |
| OECD                 | ENV/JM/MONO(2007)17                               | Guidance Document on Pesticide Residue Analytical Methods   |
| IUPAC                | <i>Pure Appl. Chem.</i> ,<br>2002, 74(5), 835–855 | Harmonized Guidelines for Single Laboratory Validation of method of analysis                      |
| HKAS<br>(HKSAR, PRC) | HOKLAS Supplementary<br>Criteria No. 37           | “Food” Test Category - Chemical Testing   |
| AQSIQ<br>(PRC)       | GB/T 27404-2008                                   | Criterion on Quality Control of Laboratories –<br>Chemical Testing of Food                        |





# Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)

## *“Guidelines on Good Laboratory Practice in Pesticide Residue Analysis”*

- Analyst
- Basic resources
- Analysis
  - **Validation of methods**
  - **Performance verification**
  - **Confirmatory tests**
  - **Mass spectrometry**
  - **Lowest calibrated level (LCL)**
  - **Expression of results**







# Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)

## *“Guidelines on Good Laboratory Practice in Pesticide Residue Analysis”*

- Parameters to be addressed in
  - **Method validation**
  - **Extension of validated method**
  - **Adaptation of validated method by another laboratory**
  - **Performance verification**
  
- **Representative commodities/samples for validation of analytical procedures**





## EU SANCO/10684/2009

### *“Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed”*

- **Analytical method validation and performance criteria**
  - Qualitative screening methods
  - Initial method validation
- **Acceptability of analytical method performance - extended method validation**
  - On-going performance verification (routine recovery determination)
  - Fat or dry weight content determination
- **Acceptability of analytical performance for routine recoveries**





## EU SANCO/10684/2009

*“Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed”*

- **Proficiency testing and analysis of reference materials**
- **Confirmation of results**
  - Identification
  - Mass spectrometry coupled to chromatography
- **Reporting of results**
  - Expression
  - Calculation
  - Rounding
  - Uncertainty



# Key Elements on Method Performance

- Accuracy / Trueness
- Precision
- Specificity & selectivity
- Limit of Detection (LOD)
- Limit of Quantitation (LOQ)



# Guidance on Accuracy / Trueness Requirements

| Analyte level   | <u>CODEX</u>   | <u>EU</u>           | <u>EU</u>           | <u>PRC(HK)</u>              |
|---|----------------|---------------------|---------------------|-----------------------------|
|   | CAC-GL 40-1993 | SANCO/10684/2009    | 2002/657/EC*        | HOKLAS Supp. Criteria No.37 |
| $\leq 1 \mu\text{g}/\text{kg}$                              | 50-120         | 70-120 <sup>1</sup> | 50-120 <sup>2</sup> | 40-120                      |
| $> 1 \mu\text{g}/\text{kg} \leq 0.01 \text{ mg}/\text{kg}$  | 60-120         |                     | 70-110 <sup>2</sup> | 60-115                      |
| $> 0.01 \text{ mg}/\text{kg} \leq 0.1 \text{ mg}/\text{kg}$ | 70-120         |                     | 80-110 <sup>2</sup> | 80-110 <sup>3</sup>         |
| $> 0.1 \text{ mg}/\text{kg} \leq 1 \text{ mg}/\text{kg}$    | 70-110         |                     |                     |                             |
| $> 1 \text{ mg}/\text{kg}$                                  | 70-110         |                     |                     |                             |

**Note:**

\* Represented as recovery ranges from certified/true/spike values for direct comparison, deviation ranges given in the actual guidance documents.

<sup>1</sup> Recoveries outside this range may be accepted for certain justified cases, typically with multi-residue methods. Mean recovery below 70% may be acceptable in exceptional case where recovery is low but consistent (i.e. demonstrating good precision) and the basis for this is well established (e.g. due to pesticide distribution in partition).

<sup>2</sup> Recovery corrected.

<sup>3</sup> More stringent requirements for levels above 100 mg/kg.



# Guidance on Precision Requirements

| Analyte level                                 | <u>CODEX</u>             | <u>EU</u>                    |
|---|--------------------------|------------------------------|
|   | CAC-GL40-1993<br>(CV, %) | SANCO/10684/2009<br>(RSD, %) |
| $\leq 1 \mu\text{g/kg}$                       | 35                       | 20                           |
| $> 1 \mu\text{g/kg} \leq 0.01 \text{ mg/kg}$  | 30                       |                              |
| $> 0.01 \text{ mg/kg} \leq 0.1 \text{ mg/kg}$ | 20                       |                              |
| $> 0.1 \text{ mg/kg} \leq 1 \text{ mg/kg}$    | 15                       |                              |
| $> 1 \text{ mg/kg}$                           | 10                       |                              |

| Analyte level        | <u>PRC</u><br>GB/T 27404-2008<br>(CV, %) |
|----------------------|--|
|                      | 0.1 $\mu\text{g/kg}$                     |
| 1 $\mu\text{g/kg}$   | 30 %                                     |
| 10 $\mu\text{g/kg}$  | 21 %                                     |
| 100 $\mu\text{g/kg}$ | 15 %                                     |
| 1 mg/kg              | 11 %                                     |
| 10 mg/kg             | 7.5 %                                    |
| 100 mg/kg            | 5.3 %                                    |
| 1000 mg/kg           | 3.8 %                                    |
| 1 %                  | 2.7 %                                    |
| 10 %                 | 2.0 %                                    |
| 100 %                | 1.3 %                                    |



# Specificity & Selectivity

- Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)
  - Analyse  $\geq 5$  blanks of each representative commodity obtained preferably from different sources. Report analyte equivalent of blank response
  - Lowest calibrated level (LCL)  $\leq 0.3 \times$  Accepted Limit (AL) (preferably, except when  $AL \geq LOQ$ )
  - Relative retention value (RRt) :  $\pm 2\%$  (GC);  $\pm 5\%$  (HPLC)



# Specificity and Selectivity

## ■ EU SANCO/10684/2009

- Response in reagent blank and control samples being less than 30% of LOQ
- Identification requirements for different types of MS

| MS Mode                          | Typical systems / example                           | Acquisition                                   | Requirements for identification   |
|----------------------------------|---|---|---|
| MS<br>(std. mass res.)           | Quad., Ion trap, TOF                                | Full scan,<br>Limited m/z range,<br>SIM       | ≥ 3 diagnostic ions<br>(preferably incl.<br>quasi-molecular ion)  |
| MS<br>(high res. /<br>high mass) | TOF, Orbitrap,<br>FTMS, Magnetic<br>sector          | Full scan,<br>Limited m/z range,<br>SIM       | ≥ 2 diagnostic ions<br>(preferably incl.<br>quasi-molecular ion).<br>Mass accuracy < 5 ppm.<br>At least one fragment ion. |
| MS/MS                            | QQQ, Ion trap,<br>Hybrid MS<br>(e.g. Q-TOF, Q-trap) | SRM/MRM,<br>Full scan product-<br>ion spectra | ≥ 2 product ions  |





# Specificity and Selectivity

## ■ EU SANCO/10684/2009

- Guidance on relative ion abundance ratio from Chromatographic – MS techniques

| Relative intensity (% of base peak) | EI-GC-MS (relative) | CI-GC-MS, GC-MS <sup>n</sup> , LC-MS, LC-MS <sup>n</sup> (relative) |
|-------------------------------------|---------------------|---|
| > 50 %                              | ± 10 %              | ± 20 %  |
| > 20 % to 50 %                      | ± 15 %              | ± 25 %  |
| > 10 % to 20 %                      | ± 20 %              | ± 30 %  |
| ≤ 10 %                              | ± 50 %              | ± 50 %  |

(Also in HOKLAS Supplementary Criteria No. 37)

- Relative retention time (RRT) :
  - ± 0.5 % (GC); ± 2.5 % (HPLC) with suitable IS
  - ± 5 % (HPLC) without suitable IS



# Limit of Detection (LOD)

- Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)
  - “Smallest concentration where the analyte can be identified. Commonly defined as the minimum concentration of analyte in the test sample that can be measured with a stated probability that the analyte is present at a concentration above that in the blank sample.”
- Codex Alimentarius : 19<sup>th</sup> Procedural Manual (2010)
  - For  $ML \geq 0.1 \text{ mg/kg}$ ,  $LOD \leq ML \times 1/10$   
For  $ML < 0.1 \text{ mg/kg}$ ,  $LOD \leq ML \times 1/5$   
(ML = specified level of a specified commodity)  
(Also in HOKLAS Supplementary Criteria No. 37)



# Limit of Detection (LOD)

- EU SANCO/10684/2009
  - Not explicitly defined
  - Adoption of a “reporting limit” at the LCL avoids the unjustifiably high cost of confirming the presence, or absence, of residues at unnecessarily low levels



# Limit of Quantitation (LOQ)

- Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)
  - “Smallest concentration of the analyte that can be quantified. Commonly defined as the minimum concentration of analyte in the test sample that can be determined with acceptable precision (repeatability) and accuracy under the stated conditions of the test.”
- Codex Alimentarius : 19<sup>th</sup> Procedural Manual (2010)
  - For  $ML \geq 0.1 \text{ mg/kg}$ ,  $LOQ \leq ML \times 1/5$   
For  $ML < 0.1 \text{ mg/kg}$ ,  $LOQ \leq ML \times 2/5$   
(ML = specified level of a specified commodity)  
(Also in HOKLAS Supplementary Criteria No. 37)



# Limit of Quantitation (LOQ)

- EU SANCO/10684/2009
  - “The **minimum** concentration or mass of the analyte that can be **quantified** with acceptable accuracy and precision. Should apply to the complete analytical method.”
  - “**Lowest validated spike level** that meets the method performance acceptability criteria”  
(mean recoveries: 70-120%, RSD  $\leq$  20%).
  - $\leq$  Reporting limit and MRL



# Selection of Representative Matrices

- Codex CAC/GL 40-1993 (Rev. 2003, Amend. 2010)

| Plant products  |  |                           |   |
|-----------------|--|---------------------------|---|
| Commodity Group | Common properties                            | Commodity class           | Representative species                    |
| I               | High water and chlorophyll content           | Leafy vegetables          | spinach or lettuce                        |
|                 |  | Brassica leafy vegetables | broccoli, cabbage, kale                   |
|                 |  | Legume vegetables         | green beans                               |
| II.             | High water and low or no chlorophyll content | Pome fruits               | apple, pear                               |
|                 |  | Stone fruits              | peach, cherry                             |
|                 |  | Berries                   | Strawberry                                |
|                 |  | Small fruits              | grape                                     |
|                 |  | Fruiting vegetables       | tomato, bell pepper, melon                |
|                 |  | Root vegetables           | Mushroom<br>potato, carrot, parsley,      |
| III.            | High acid content                            | Citrus fruits             | orange, lemon                             |
| IV.             | High sugar content                           |                           | raisins, dates                            |
| V.              | High oil or fat                              | Oil seeds                 | avocado, sunflower seed                   |
|                 |  | Nuts                      | walnut, pecan nut, pistachios             |
| VI.             | Dry materials                                | Cereals                   | wheat, rice or maize grains               |
|                 |  | Cereal products           | wheat bran, wheat flour                   |
|                 | Commodities requiring individual test        |                           | e.g. garlic, hops, tea, spices, cranberry |

| Products of animal origin |                   |                 |                           |
|---------------------------|-------------------|-----------------|---------------------------|
| Commodity Group           | Common properties | Commodity class | Representative species    |
|                           | ---               | Meats           | Cattle meat, chicken meat |
|                           | ---               | Edible offals   | Liver, kidney             |
|                           | ---               | Fat             | Fat of meat               |
|                           | ---               | Milk            | Cow milk                  |
|                           | ---               | Eggs            | Chicken egg               |



# Selection of Representative Matrices

- EU SANCO/10684/2009

| Vegetables, fruits and cereals |                                     |  |
|--------------------------------|-------------------------------------|--|
| Commodity groups               | Commodity categories                | Typical representative commodities included in the category                              |
| High water content             | Pome fruit                          | Apples, pears  |
|                                | Stone fruit                         | Apricots, cherries, peaches  |
|                                | Bulb vegetables                     | Bulb onion   |
|                                | Fruiting vegetables/cucurbits       | Tomatoes, peppers, cucumber, melon   |
|                                | Brassica vegetables                 | Cauliflower, Brussels sprout, cabbage, broccoli  |
|                                | Leafy vegetables and fresh herbs    | Lettuce, spinach, basil  |
|                                | Stem and stalk vegetables           | Leek, celery, asparagus  |
|                                | Forage/fodder crops                 | Fresh alfalfa, fodder vetch, fresh sugar beets   |
|                                | Fresh legume vegetables             | Fresh peas with pods, petit pois, mange tout, broad bean, runner bean, dwarf French bean |
|                                | Leaves of root and tuber vegetables | Sugar beet and fodder beet tops  |
|                                | Fresh Fungi                         | Champignons, chanterelles  |
|                                | Root and tuber vegetables or feed   | Sugar beet and fodder beet roots, carrot, potato, sweet potato                           |

# Selection of Representative Matrices

- EU SANCO/10684/2009

| Vegetables, fruits and cereals                               |                                   |   |
|--|-----------------------------------|---|
| Commodity groups   | Commodity categories              | Typical representative commodities included in the category   |
| High oil content   | Tree nuts                         | Walnut, hazelnut, chestnut  |
|  | Oil seeds and products thereof    | Oilseed rape, sunflower, cotton- seed, soybeans, peanuts, sesame etc. Oils and pastes (e.g. peanut butter, tahina) thereof, |
|  | Oily fruits and products          | Olives, Avocados and oils and pastes thereof  |
| High starch and/or protein content & low water & fat content | Dry legume vegetables/pulses      | Field bean, dried broad bean, dried haricot bean (yellow, white/navy, brown, speckled)                                      |
|  | Cereal grain and products thereof | Wheat, rye, barley and oat grain; maize, rice, wholemeal bread, white bread, crackers, breakfast cereals, pasta             |
| High acid content & high water content                       | Citrus fruit                      | Lemons, mandarins, tangerines, oranges  |
|  | Small fruit and berries           | Strawberry, blueberry, raspberry, Black currant, red currant, white currant, grapes   |
|  | Other                             | kiwifruit, pineapple, rhubarb   |
| High sugar & low water content                               | Dried fruit                       | Raisins, dried apricots, dried plums, fruit jams  |
| "Difficult or unique commodities"*                           |                                   | Hops Cocoa beans and products thereof, Coffee, Tea Spices   |



# Selection of Representative Matrices

- EU SANCO/10684/2009

| Products of animal origin |                      |   |
|---------------------------|----------------------|---|
| Commodity groups          | Commodity categories | Typical representative commodities included in the category |
| Meat                      | Red meat             | Beef, pork, lamb, game, horse                               |
|                           | White meat           | Chicken, duck, turkey                                       |
|                           | Fish                 | Cod, haddock, salmon, trout,                                |
|                           | Offal *              | Liver, kidney   |
|                           | fat from meat        |   |
| Milk & milk products      | Milk                 | Cow, goat and buffalo milk                                  |
|                           | Cheese               | Cow, goat cheese  |
|                           | Yogurt               |   |
|                           | Cream                |   |
|                           | Butter               |   |
| Eggs                      | Eggs                 | Chicken, duck, quail, goose eggs                            |
| Honey                     | Honey                |   |

\* Offal (liver, kidney) should be validated separately, if necessary



**Thank you**



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Analytical Performance Criteria  
Approach in Pesticide Residues  
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