The Community Reference Laboratory for GM Food and Feed

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What are your needs regarding the set-up of enforcement laboratories
Taking into account the information of this workshop?

How could those needs be met?

In which way could the JRC/European Commission support you?

Contact: jrc-bgmo@ec.europa.eu

Why Validation Studies ?

- Conducting a validation study is a tool to check whether the method is *fit for the purpose*
- The validation study delivers *performance characteristics*

How to validate the analytical method?

  - By performing an in-house validation
  - By conducting a collaborative study

The Community Reference Laboratory for GM Food and Feed: two legal mandates

1) Community Reference Laboratory for GM Food and Feed (CRL-GMFF) under Regulation (EC) 1829/2003.

2) Community Reference Laboratory for Genetically Modified Organisms (CRL-GMO) under Regulation (EC) No 882/2004 on “official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules”.

Duties and tasks of the CRL-GMFF as defined by Reg. (EC) No 1981/2006

a) the reception, preparation, storage, maintenance and distribution to the members of the European Network of GMO laboratories of the appropriate positive and negative **control samples**….

(b) without prejudice to the responsibilities of the Community reference laboratories laid down in Article 32 of Regulation (EC) No 882/2004… the **distribution** to national reference laboratories within the meaning of Article 33 of that Regulation of the appropriate positive and negative control samples….

(c) **evaluating** the data provided by the applicant for authorisation for placing the food or feed on the market, for the purpose of testing and validation of the method for sampling and detection;

(d) **testing and validating** the method for detection, including sampling and identification of the transformation event and, where applicable, for the detection and identification of the transformation event in the food or feed;

(e) submitting **full evaluation reports** to the Authority.

The CRL-GMFF

- **Official mandate** in the EU regulatory process, based upon recognition of existing expertise in JRC/ENGL.
- Operations are carried out in parallel with the **European Food Safety Authority** (EFSA).
- It has a crucial role in (**dis)approval of methods** that are “fit for the purpose of regulatory compliance”.
- It has a key role in **disputes** and in response to **crises.**
- It is **unique** in the worlds’ GMO regulatory system.
- >80 **dossiers** have been submitted to the CRL-GMFF since April 2004.
- Applicants contribute to the **costs of validation** (Reg. No 1981/2006).
- It is **ISO 9001** certified and **ISO 17025** accredited.
- All methods validated and validation reports are published at http://gmo-crl.jrc.ec.europa.eu/

The CRL-GMFF

“ For the tasks outlined in this Annex, the Commission's Joint Research Centre shall be assisted by a consortium of National Reference Laboratories, which will be referred to as the **‘European Network of GMO laboratories.’**

The CRL-GMO: tasks as outlined by Article 32 of Reg. (EC) No 882/2004

Assisting the National Reference Laboratories (NRLs) in their duties to monitoring the European market in a context of health and consumer protection with three main objectives:

- Solving scientific issues related to **harmonisation and communication** of scientific data among laboratories;
- **Monitoring** the quality levels of the analytical laboratories for GMO detection;
- Building capacities through **training**, workshops and any common scientific normative tool available.

Standards for Method Validation

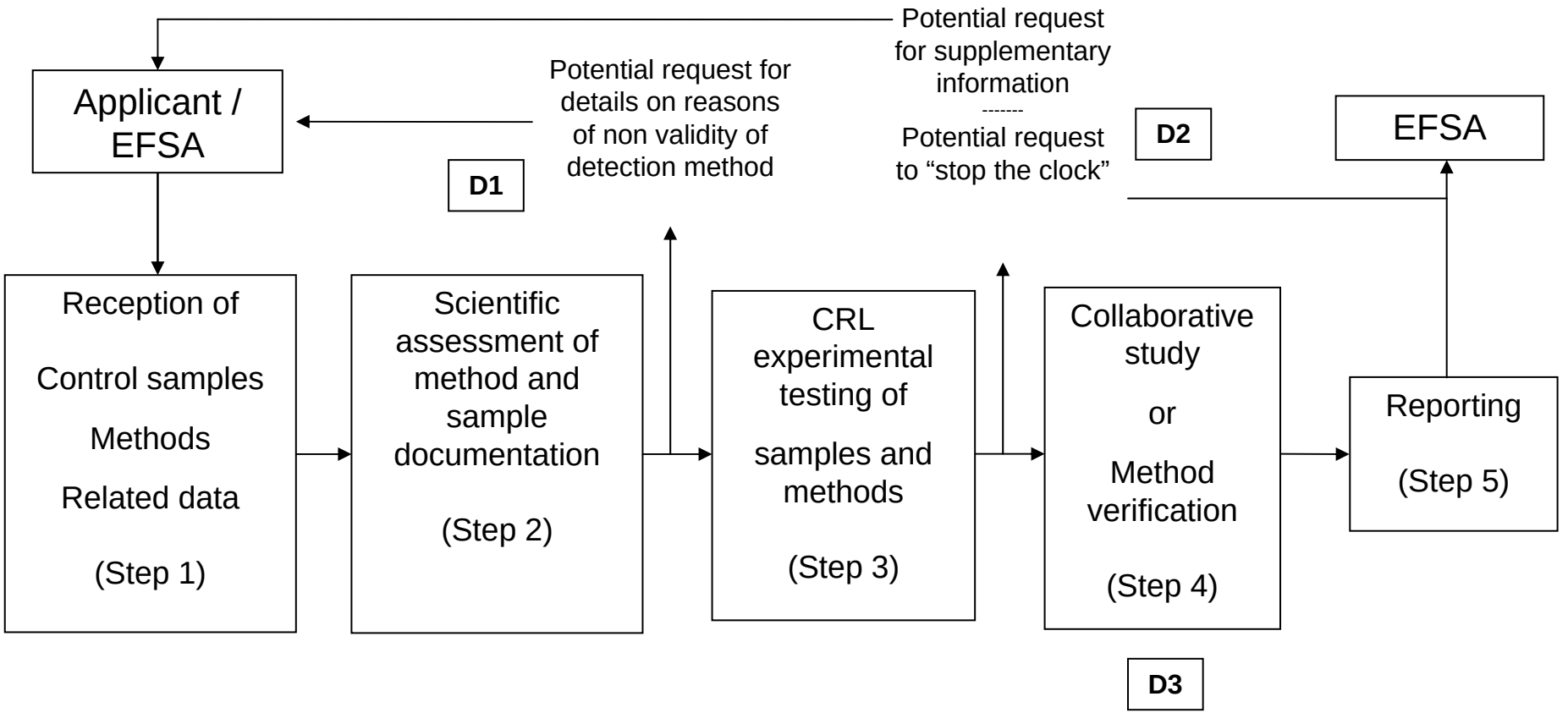
- ENGL: Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing – Version 13/10/2008
- ISO 5725 – Accuracy (trueness and precision) of measurements methods and results
- IUPAC, 1995 – Protocol for the Design, Conduct and Interpretation of Method-Performance Studies
- Codex Alimentarius Commission - Consideration of the methods for the detection and identification of foods derived from biotechnology general approach and criteria for the methods. Accepted 2008.
- Codex Alimentarius Commission – Single Laboratory Validation – Consideration of Harmonized IUPAC guidelines for Single-Laboratory Validation of Methods of Analysis

Regulation (EC) No 641/2004 of 6 April 2004 on detailed rules for GM food and feed legislation

- Method acceptance criteria and method performance requirements: ENGL/CRL guidance document “Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing”
- Information about the method: **event-specificity**, applicability, detailed description of the methods etc.
- Information about method testing carried out by the applicant: method optimisation, inter-lab transferability, stability, specificity, LOD, LOQ etc, testing report
- **Full sequence of the insert(s) + flanking sequences**
- Control samples and samples of food and feed

For all info see: http://gmo-crl.jrc.it

CRL-GMFF operational procedures



The process is a step-by-step procedure and can be stopped or re-initiated as required

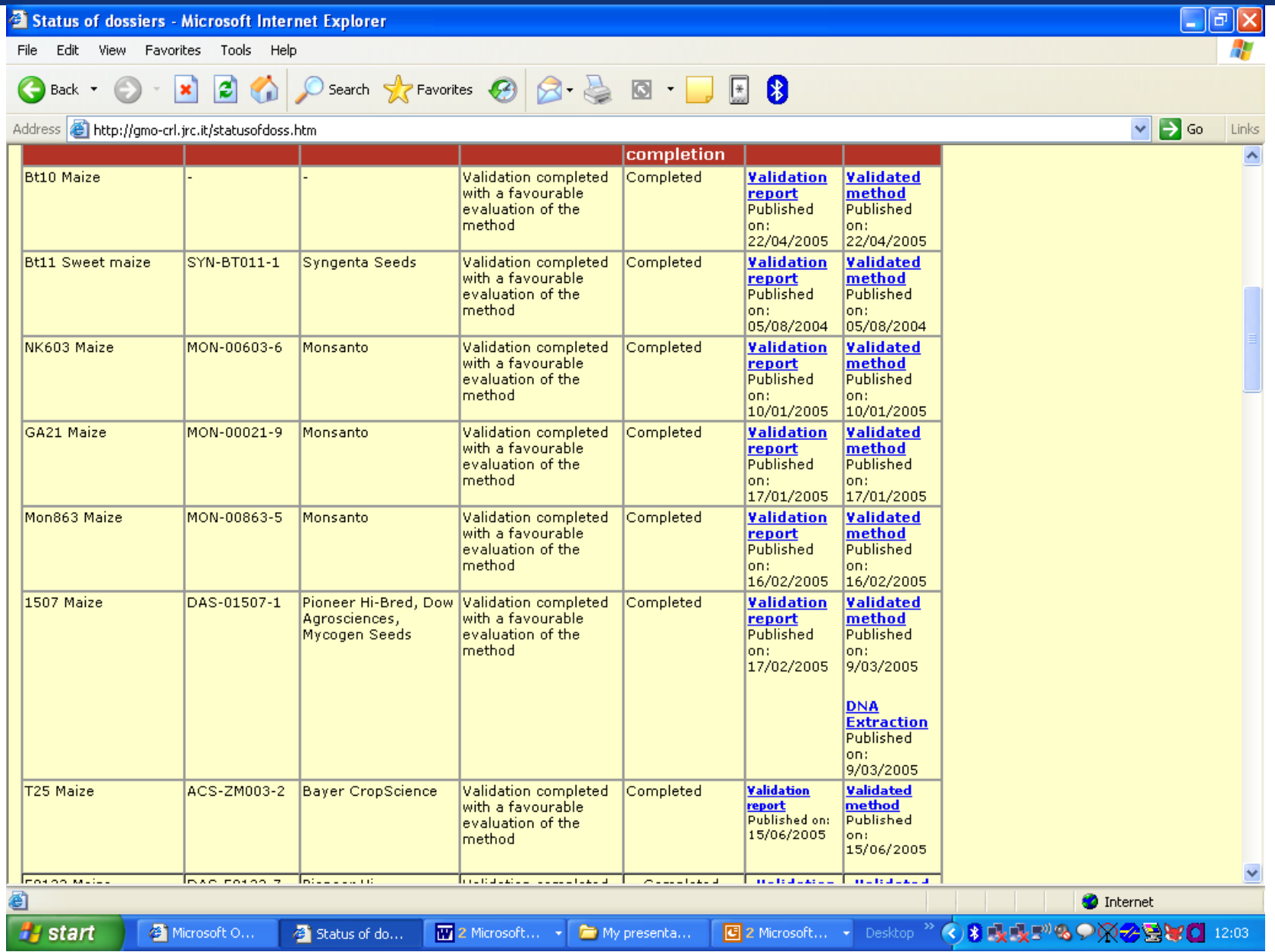
Methods minimum performance requirements: CRL-GMFF acceptance criteria and performance requirements (http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm)

Applicability	Scope of the method, interferences with analytes etc.
Practicability	Equipment, timing, practical difficulties
Specificity	Event-specificity
Dynamic Range	Include the 1/10 and at least 5 times the target concentration
Accuracy	Within ± 25% of the reference value
R^2 Coefficient	≥ 0.98
PCR efficiency	- 3.1 ≥ slope ≥ 3.6
RSDr	Below 25% over the whole dynamic range
LOQ	Less than 1/10th of the value of the target concentration with an RSDr ≤ 25%
LOD	Less than 1/20th of the target concentration
Robustness	Deviate not more than ± 30%
RSDR	Below 35% at the target concentration; < 50% below 0.2%
Trueness	Within ± 25 of the accepted reference value over the whole range

TESTING METHOD INTER-LABORATORY PERFORMANCE: Example of the CRL-GMFF validation of a method for regulatory compliance: TC1507 *Herculex* maize "fit for the purpose"

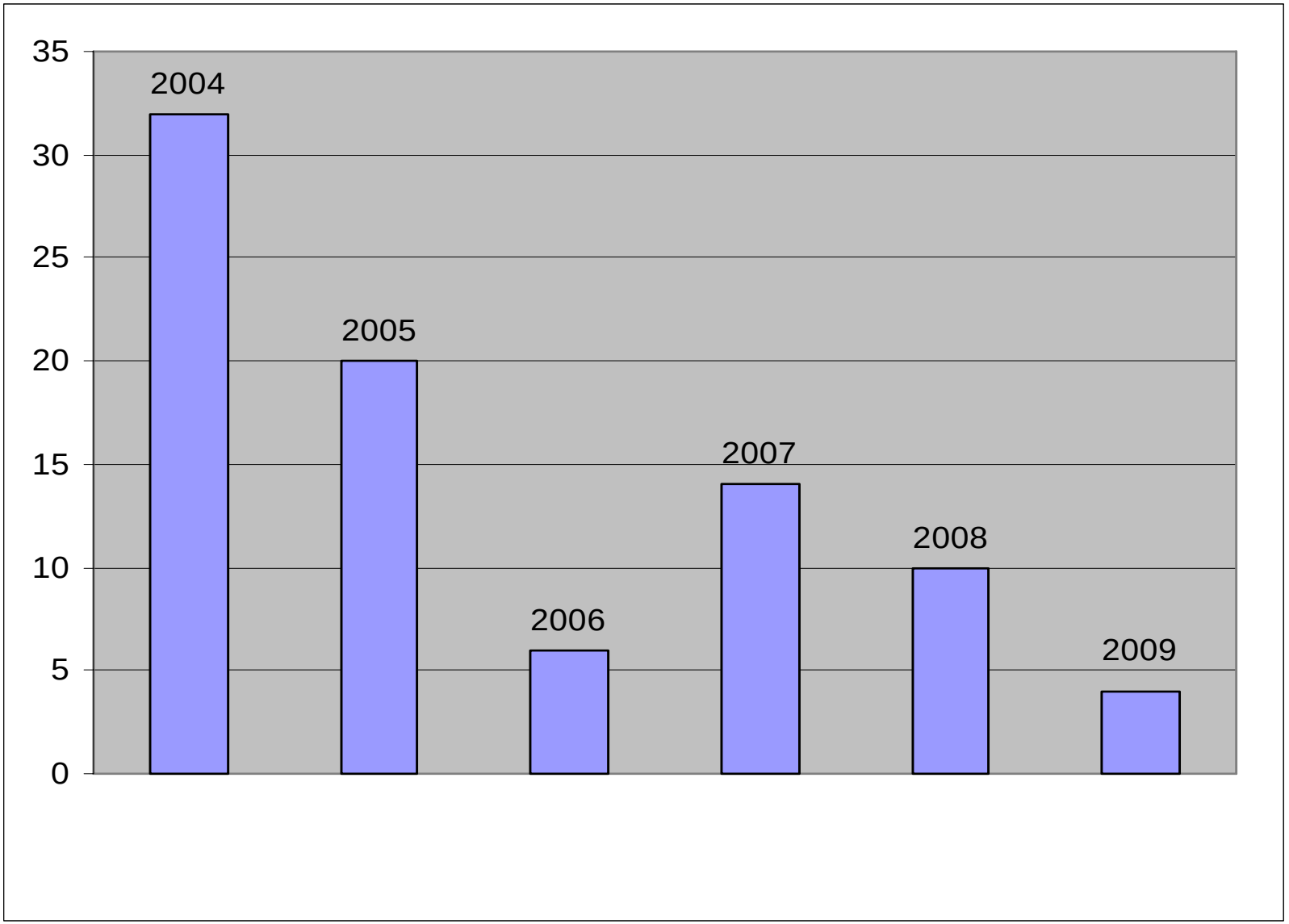
Validation 1507 (*Herculex™ I* – Pioneer) maize

Sample	0.00	0,1	0,5	0,9	2	5
Number of laboratories	14	14	14	14	14	14
Number of outliers	0	0	1	2	1	0
Number of laboratories retained after eliminating outliers	14	14	13	12	13	14
Mean value	0,000	0,106	0,480	0,933	1,966	5,420
Bias (%)	0	6	-4	4	-2	8
Repeatability standard deviation s_r	0,00	0,02	0,06	0,07	0,17	0,78
Repeatability relative standard deviation RSD_r (%)	0,00	18,11	11,70	7,68	8,48	14,41
Repeatability limit r ($r = 2.8 \times s_r$)	0,00	0,05	0,16	0,20	0,47	2,19
Reproducibility standard deviation s_R	0,00	0,02	0,07	0,10	0,42	1,17
Reproducibility relative standard deviation RSD_R (%)	0,00	19,91	14,78	10,24	21,19	21,65
Reproducibility limit R ($R=2,8 \times s_R$)	0,00	0,06	0,20	0,27	1,17	3,29



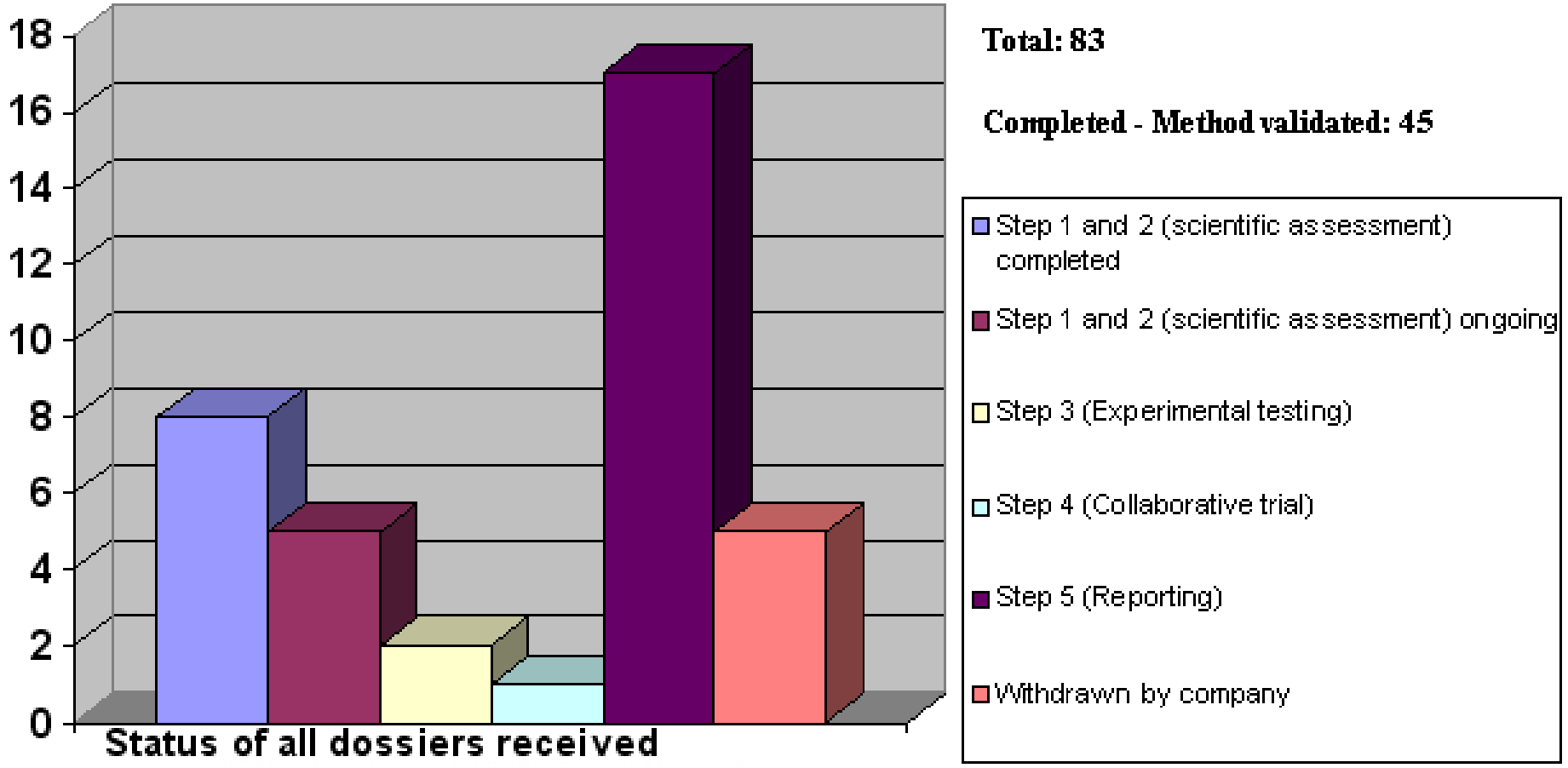
				completion		
Bt10 Maize	-	-	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 22/04/2005	Validated method Published on: 22/04/2005
Bt11 Sweet maize	SYN-BT011-1	Syngenta Seeds	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 05/08/2004	Validated method Published on: 05/08/2004
NK603 Maize	MON-00603-6	Monsanto	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 10/01/2005	Validated method Published on: 10/01/2005
GA21 Maize	MON-00021-9	Monsanto	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 17/01/2005	Validated method Published on: 17/01/2005
Mon863 Maize	MON-00863-5	Monsanto	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 16/02/2005	Validated method Published on: 16/02/2005
1507 Maize	DAS-01507-1	Pioneer Hi-Bred, Dow Agrosciences, Mycogen Seeds	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 17/02/2005	Validated method Published on: 9/03/2005 DNA Extraction Published on: 9/03/2005
T25 Maize	ACS-ZM003-2	Bayer CropScience	Validation completed with a favourable evaluation of the method	Completed	Validation report Published on: 15/06/2005	Validated method Published on: 15/06/2005

Applications submitted to CRL-GMFF by year



CRL-GMFF process update

Dossiers in CRL:



The role of the CRL-GMFF in response to emergencies and crises related to the spread of GMOs into the EU market

The CRL-GMFF has become a key actor in emergency/crises cases for fast validation/verification of detection methods, gathering and provision of specific information to NRL (e.g. sequence, molecular structure), preparation and distribution of suitable control samples to NRL.

- Decision 2005/317/EC on emergency measures regarding the non-authorised genetically modified organism Bt10 in maize products
- Decision 2006/754/EC on emergency measures regarding the non-authorised genetically modified organism LLRICE601 in rice products
- Draft Decision 2008/289/EC on emergency measures regarding the non-authorised genetically modified organism Bt63 in rice products

Thank you for your kind attention

http://bgmo.jrc.ec.europa.eu/