



# “What after the moratorium? Main changes: new guidelines in EU Regulation 641/2004

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*DG Joint Research Centre*



# The Mission of the JRC



The JRC provides customer-driven scientific and technical support for the conception, implementation and monitoring of EU policies.

The JRC functions as a reference centre of science and technology for the Union.

The JRC serves the common interest of the Member States, while being independent of special interests, whether private or national.

# The Mandate of the B&GMOs Unit

The Biotechnology & GMOs Unit is the JRC reference for the provision of scientific and technical support to policy development under the EC regulatory framework for Genetically Modified Organisms (GMOs) and for the development of biotechnology expertise in areas relevant to health and consumer protection.

It exercises the mandate of Community Reference Laboratory for GM Food and Feed.



## EU Policy Basis: where we are in 2004

- Horizontal Directive **01/018/EC** (DG ENV) on deliberate release and marketing of genetically modified organisms (GMOs);
- The vertical Regulation (EC) **No 1829/2003** of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed (DG SANCO) nominates the JRC as Community Reference Laboratory;
- Regulation (EC) **No 1830/2003** of the European Parliament and of the Council of 22 September 2003 concerning the traceability and labeling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC (DG SANCO and DG ENV);
- The Cartagena Protocol entered into force on September 11th 2003 (DG ENV);
- Upcoming issue for the new Commission: definition of thresholds for tolerance of GM contamination in seeds.



# Regulation (EC) No1829/2003 on GM Food and Feed

Regulation 1829/03 on GM Food and Feed (Annex):

“ The Community Reference Laboratory referred to in Article 32 is the Commission's Joint Research Centre.”

And:

“ 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 European Network of GMO Labs



- Inaugurated in 2002 but started in 1999 as a spontaneous association of laboratories to solve technical issues;
- All 25 EU are participant and others (e.g. Rumania, Bulgaria, Turkey etc.) are participating observers;
- Today >75 enforcement laboratories, appointed by national competent authorities;
- Links with Asia – (North) Africa etc.;
- Harmonisation of enforcement procedures, e.g. uniform sampling procedures – uniform expression of data – uniform interpretation of thresholds – tailored reference materials, training and capacity building....



## Duties and tasks of the CRL as defined by Reg. (EC)1829/2003:

- Reception, preparation, storage, maintenance and distribution to national reference laboratories of the appropriate positive and negative control samples;
- Testing and validation of the method for detection, including sampling and identification of the transformation event.....in the food or feed;
- Evaluating the data provided by the applicant for authorisation for placing the food or feed on the market...;
- Submitting full evaluation reports to the Authority.
- The Community reference laboratory shall play a role in dispute settlements.



## **Commission Regulation (EC) No 641/2004 of 6 April 2004 on implementing rules for GM food and feed legislation**

- Annex 1: Method Validation
- 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



## Regulation (EC) No 641/2004: Samples Provided by the Applicant

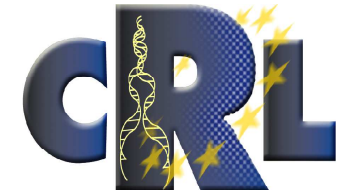
- Control samples (validation of PCR module)
  - The GMO or its genetic material
  - The GMO (100%) and the the wt must be provided
- Samples of food/feed (testing/validation of DNA extraction module)
  - The material for which the authorisation of the event is submitted (i.e. seeds, grains, marmalade, chocolate bar)
  - Should contain the GMO at min. content of 0.9%
  - If analyte is not significantly present (i.e. refined oil), the first material upstream in the processing



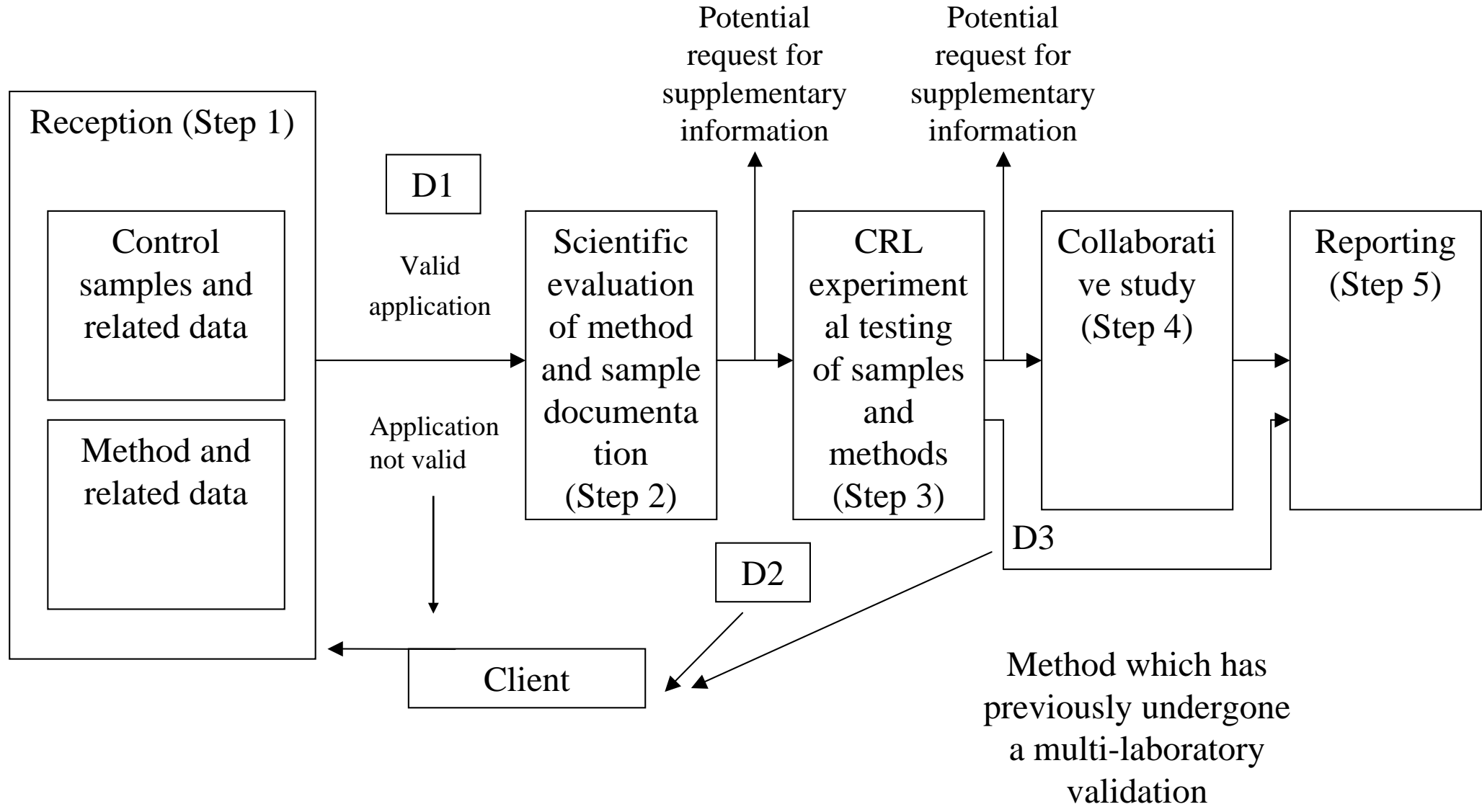
## Guidance documents made available by the CRL <http://gmo-crl.jrc.it>

- Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing
- Explanatory Notes to Applicants: provide the applicants with practical instructions concerning the method validation task of the CRL as described Regulation (EC) 1829/2003 and in the Regulation (EC) 641/2004
- Format to provide information, protocol template, description of the CRL validation process

# CRL operational procedures



Joint Research Centre



# The Community Reference Laboratory

- Operations are carried out in parallel with the European Food Safety Authority
- Thirty-five dossiers have been submitted to the CRL since April 2004
- All dossiers were managed according to CRL Operational Procedures and the Quality Management System in place.
- For all dossiers a scientific evaluation of the documentation (methods and samples) was carried out and official comments were submitted to EFSA and DG SANCO.
- Five validations have been completed, reports and methods published; at this moment at least three inter-lab studies are in preparation



# The Community Reference Laboratory

- Accreditation ISO 17025 and Certification ISO 9001
- 14 staff, including scientific officers, lab technicians, quality manager, IT support, biometrician, secretariat.
- Laboratory facilities to increase in 2005/2006



## Example of the validation of a method for regulatory compliance: Bt 11 sweet maize “fit for the purpose”

<b>Unknown sample GM%</b>	<b>0.1</b>	<b>0.3</b>	<b>0.7</b>	<b>1.0</b>	<b>1.3</b>	<b>2.0</b>
Number of accepted samples	22	22	24	20	24	20
Mean value	0.1	0.3	0.7	1.0	1.2	1.8
Median value	0.1	0.3	0.7	1.0	1.2	1.9
Coefficient of variation (CV%)	33.4	17.7	21.5	12.1	27.0	18.5
Reproducibility relative standard deviation $RSD_R$ (in %)	33.5	19.0	24.4	12.7	27.0	18.4



## Recommendations for Sampling

- The JRC has worked out Recommendation 2004/787/EC on “technical guidance for sampling and detection of GMOs and material produced from GMOs as or in products in the context of Regulation (EC) N 1830/2003”.
- Proposed a new Unit of Measurement: “Results of quantitative analysis should be expressed as the percentage of GM-DNA copy numbers in relation to target taxon specific DNA copy numbers calculated in terms of haploid genomes”



## “Conclusions ENGL Members Meeting 13 – 14 Jan 2005”

The new accepted unit for measurement and expression of a GMO content is the most coherent approach, as it solves a lot of problems. If reference materials are used that allow to quantify and calculate a GMO content in terms of haploid genomes, and if no further translation to % GM material is needed, then the earlier mentioned biological factors do not longer present a problem. **The DNA copy number unit is the only correct, indisputable and unambiguous way of expressing a measured content of GMO.** The haploid genome is a traceable unit throughout the agricultural/food production chain.

It will clear away possible misinterpretations and make sure that results on the same sample, obtained by different laboratories, are comparable. (*I. Taverniers*)



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*GMO releases notified under Directive 2001/18/EC, can be consulted at <http://gmoinfo.jrc.it>*

**Visit the new <http://gmotraining.jrc.it> website, dedicated to training courses on detection techniques for Genetically Modified Organisms (GMOs) in foods.**

**Overview**

The pace of scientific and technological change in biotechnology has been very high over the last two decades. Scientists and technologists are increasingly exploiting the potential of biotechnology to deliver new medicines, [improved food quality](#), [environmental benefits](#), disease prevention and reduce health risks.

The European Commission has developed a broad legislative framework to ensure that GMOs and GMO-derived products that are grown, marketed and imported meet the highest standards of safety for the environment, as well as for human and animal health. Regulation needs to be enforced uniformly and effectively across the EU and the process of implementation requires critical measures such as access to validated methods and technical guidance for detection and sampling.

The European Commission's Joint Research Centre (JRC), acting via its [Institute of Health and Consumer Protection \(IHCP\)](#), and more particularly the "Biotechnology and GMOs Unit" has the mandate to provide scientific support for the development and implementation of the EU biotechnology regulations and is playing a leading role in the harmonisation of technical GM-issues.

Setting up and coordinating the European Network of GMO Laboratories, ([ENGL](#)) is considered as one of the major achievements of the JRC in recent years. ENGL constitutes a unique platform for experts from EU Member States, EEA countries and Accession Countries to discuss technical issues related to sampling, detection, identification and quantification of GMOs. The Commission that has adopted on July 25th 2001 a proposal in which the JRC, assisted by ENGL, is designated as Community Reference Laboratory for the GMO food and feed regulation has recognized the importance and value of ENGL.

In support of the Commission policy, the Biotechnology and GMOs Unit provides specific services to various Commission Services, such as:

- The reception of all summary notifications of deliberate field trials (SNIFs), notified under the deliberate release [Directive 2001/18/EEC](#);
- The weekly updates of the [SNIE](#) database, providing information to the general public of all field trials carried out in the EU;
- Participation as nominated expert in the development of an operational [Biosafety Clearing House](#).

In support of ENGL, the Unit has built up an outstanding [molecular biology expertise and facilities](#), mainly devoted to the development and the validation of methods for GMO detection and quantification. Significant efforts have been devoted to the understanding of [sampling](#) problems related to GM detection and quantification in food and raw materials. It shares its expertise and facilities for the purpose of training as it is jointly organising a number of [training courses](#) with the [World Health Organisation](#). Results obtained are not only transferred to ENGL, but also to international standardisation bodies such as CEN.

As horizontal support, a core informatics activity has been built up to:

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Record 1 Total Records: 229 Next

Method name DMIF-GEN-TIA

Purpose  Screening  Identification  Quantification

Altered Trait Delayed fruit ripening

**General data**

Species *Lycopersicon esculentum* Common crop tomato

Matrix type raw tomato

Event ID Tomato Nema282F

Company Zeneca

Assay type DNA (PCR)

Commercial Kit  Yes  No

**Validation data**

Study date 1998

Nr of Labs 19

Nr of Labs used 18

Nr samples total

Nr samples per lab

RSDReproducibility

RSDRepeatability

LOD

LOD

Specificity 100%

Sensitivity 100%

Range to

Linearity

Accuracy

Robustness

Standard status National

Coordinator Manuela Schultze, Staatliches

Country DE

Report reference EU-Project SMT4-CT96-2072. Developments of Methods to Identify Foods Produced by Means of Genetic Engineering. Final Report DMIF-GEN SMT4-CT96-2072  
method published in the official collection of methods under article 35 of the German Federal Foodstuffs Act L-25.03.01-1 (1999)

**PCR**

PCR assay Single

Thermocycler model not specified

Target genetic element description polygalacturonase (PG) gene and nos terminator

Primer sequence forward PG34L 5'-ggATCCTTAGAAGCATCTAGT-3'

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## Deliberate releases and placing on the EU market of Genetically Modified Organisms (GMOs)

The purpose of this web site, managed by the [Joint Research Centre](#) of the [European Commission](#) on behalf of the [Directorate General for the Environment](#) is to publish information and to receive comments from the public regarding notifications about deliberate field trials and placing on the market of genetically modified organisms, as defined in [Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001](#).

- Click [here](#) for more information.
- Visit the [Biotechnology and GMOs Unit](#) website.
- [Links](#)

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Download the SNIF application form in <a href="#">Word</a> or <a href="#">RTF</a> format <a href="#">List of Main Traits</a>	Download the SNIF application form in <a href="#">Word</a> or <a href="#">RTF</a> format <a href="#">List of Main Traits</a>	

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# Training Courses




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The European Commission (DG Joint Research Centre, Biotechnology and GMOs Unit) and the World Health Organisation ([WHO Food Safety Programme in Europe](#)) have collaborated since 2000 in the organisation of training courses on detection techniques for Genetically Modified Organisms (GMOs) in foods. The aim is to provide analytical biotechnology skills to food control laboratory staff and to promote the use of validated and harmonised methods for detecting, identifying and quantifying GMOs.

This site is an extension of that collaboration and aims at providing up-to-date information about the ongoing training programmes. In addition, here we provide on-line access to the latest version of the training manual used.

Click [here](#) to read the introduction to the manual  
Click [here](#) to read the introductory remarks from the World Health Organization



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**ENGL** EUROPEAN NETWORK  
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**[ENGL Inauguration Ceremony and Stakeholders' Meeting](#)**

**[Brussels, 4 December 2002](#)**



[Scientific and technical comments invited to the validation criteria document](#) 

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The European Network of GMO Laboratories (ENGL) is set up to contribute more effectively to the European harmonisation and standardisation of means and methods for sampling, detection, identification and quantification of Genetically Modified Organisms or derived products in a wide variety of matrices, covering seed, grains, food, feed and environmental samples. As such, it is aimed to act as a scientific and technical European Union network of excellence within the context of EU GMO regulation. Projects of excellence and innovation and rapid exchange of data within its members are key to ENGL.

The network was inaugurated in Brussels on December 4th in the presence of Research Commissioner Ph. Busquin and of the Director General of the [Joint Research Centre \(JRC\)](#), B. Mc Sweeney.

It currently consists of 44 EU enforcement laboratories, plus Norway and a number of observers such as Accession Countries.

The chairmanship of the network is under the responsibility of the unit "[Biotechnology and GMOs](#)" of the JRC's [Institute for Health and Consumer Protection](#).

The scope is to create a unique platform for experts that are involved in the sampling, detection, identification and quantification of GMO's - being in the environment, food, feed and seeds - and where technical items can be put forward and discussed, namely:

- Method development for qualitative and quantitative analysis;
- Molecular biology technology transfer;
- Validation and proficiency studies of methods suitable either for screening of various matrices for the presence of GMO's, or for the estimation of the GMO quantities present;
- Reference material (the responsibility for this work package lies with the JRC's [Institute for Reference Materials and Measurements](#));
- [Sampling](#) strategies and procedures for different GM-commodities (seeds, grains, raw material, products for final consumer or mass caterers);
- Databases and bioinformatics and requirements for unique identification of GMO's and setting up of databases that contain these molecular data;
- Training has been organized at the Ispra site.

A restricted Web site, the "[Bulletin Board of the European Network of GMO Laboratories](#)", has been set up with the purpose to facilitate exchange of information, post notices and view information on news and events.




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## Status of dossiers

**CRL validation processes**

[Click here to access to the detection methods submitted under Art 47 of regulation EC No 1829/2004](#)

The following table lists the CRL validation processes within the frame of the Regulation 1829/2003. The JRC has anticipated the CRL activities by launching some studies as early as 2003. These are carried out according to the same scientific, international standards as the studies from the official date of the CRL. The full method reports will be made available after the authorization process has been completed.

The GM events for which the CRL is validating a detection method may have been notified for several purposes at the same time (for instance within the Regulation 2001/18/EC). The following links provide information about the authorization procedures, notifications and opinions granted by the European Food Safety Agency (EFSA).

[European Commission information on GM authorizations, legislation and alike](#)

[Information about the notifications submitted in the context of Directive 2001/18/EC](#)

[Opinions of the EFSA Scientific Panel on Genetically Modified Organisms](#)

[Register of requested opinions from EFSA](#)

Event	Unique identifier	Applicant	Status/Progress	Expected date of completion	Reports
Bt11 sweet maize	SYN-BT011-1	Syngenta Seeds	Completed with a favorable evaluation for the method.	Completed in October 2003	<a href="#">Summary</a> The method report will be made available after the authorization process has been completed.
NK603 Maize	MON-00603-6 (proposed)	Monsanto	Step 4: Collaborative study.	May 2004	-
GA21 Maize	MON-00021-9	Monsanto	Step 4: Collaborative study.	June 2004	-
Mon863 Maize	MON-00863-5	Monsanto	Step 2 completed (scientific evaluation of the method and sample documentation).	Second half of 2004	-
T25 maize	ACS-ZM003-2	Bayer CropScience	Waiting material delivery.	Second half of 2004	-
1507 Maize	DAS-	Pioneer Hi-Bred, Dow	Waiting material delivery.	Second half of	-

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# Further Information

- <http://biotech.jrc.it> (overview of the biotechnology activities)
- <http://engl.jrc.it> (the European Network of GMO Laboratories)
- <http://gmotraining.jrc.it> (information about the training activities)
- <http://gmoinfo.jrc.it> (overview of field releases and of products notified on the EU market)
- <http://gmo-crl.jrc.it> (the CRL web-site)