

BIONale 2004, Maastricht, 2 November 2004

**EUROPEAN ROUND TABLE ON REGULATIONS  
FOR LIFE SCIENCES AND BIOTECHNOLOGY**

**ANNEX TO DISCUSSION PAPER**

final version

26 October, 2004

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## 1. INTRODUCTION TO THE FOUR KEY DOCUMENTS

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The discussion paper aims at facilitating an exchange of views between the participants at the European Round Table on Biotechnology Regulations at BIONale 2004 on the needs and priorities for action with a view to further adapt and/or complete the European regulatory framework for healthcare biotechnology and agro-food biotechnology. In order to identify potential needs and priorities for further action, this Annex to the discussion paper starts by a review of the current state of affairs. Starting points for this review include four key documents:

- The Commission's communication<sup>1</sup> of 2002 for European strategy for life sciences and biotechnology: A detailed strategic action plan was spelled out, which aims at enhancing Europe's competitiveness in the global market place, in line with the Lisbon 2010 goal. The Action Plan included a series of actions to strengthen confidence in science-based regulatory oversight and to complete the regulatory framework for healthcare biotechnology and agro-food biotechnology.
- The report<sup>2</sup> of 2003 of the Competitiveness in Biotechnology Advisory Group with Industry and Academia (CBAG): The CBAG, which was set up accordance with Action 10b of the Action Plan to provide input into the Commission's annual report on the implementation of the Strategy, issued its first report in 2003. The CBAG chose to concentrate on financial and regulatory issues. As regards regulatory issues, several specific recommendations were made by the CBAG.
- The Commission's second progress report<sup>3</sup> of 2004 on the implementation of the strategy: An overview was presented of the progress made with the review of pharmaceutical legislation and the adoption, implementation and enforcement of GMO legislation, whereby several priorities for future action by the Commission and Member States were identified.
- The conclusions<sup>4</sup> adopted by the Competitiveness Council at the meeting of 17 and 18 May 2004 on approaches to better regulation, including impact assessment of new Community legislation.

The review is further informed by documentation made available at websites of various Commission services, Community research institutions, the European Agency for the

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<sup>1</sup> Life Sciences and biotechnology – A Strategy for Europe, Communication from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions, COM(2002) 27 final, 23.1.2002.

<sup>2</sup> Competitiveness in Biotechnology Advisory Group – Report 2003.

<sup>3</sup> Life Sciences and biotechnology – A Strategy for Europe: second progress report and future orientations, Communication from the Commission to the Council, the European Parliament and the Economic and Social Committee, COM(2004) 250 final, 07.04.2004.

<sup>4</sup> 2583<sup>rd</sup> Council Meeting Competitiveness (Internal Market, Industry and Research), C/04/140, Brussels, 17 and 18 May 2004.

Evaluation of Medicinal Products (EMA), and the European Food Safety Authority (EFSA), as well as of Europabio, the European association of bioindustries.

The findings of the review are reported in the three following chapters. While Chapter 2 aims at identifying potential regulatory needs and priorities for action in the area of healthcare biotechnology, Chapter 3 aims at identifying potential regulatory needs and priorities for action in the area of agro-food biotechnology. Finally, Chapter 4 provides a concise review of the implementation and coherence of both EU regulatory frameworks for healthcare biotechnology products and for agro-food biotechnology products across policies, sectors and actors.

## 2. LEGISLATION FOR HEALTHCARE BIOTECHNOLOGY

### 2.1 State of affairs according to three key documents

The table below summarises and compares Action 18 of the Commission's Strategy Action Plan of 2002, the recommendations of 2003 by the CBAG for adaptation of the regulatory framework for healthcare biotechnology applications and the progress made according to Commission's second progress report.

Action plan (2002)	CBAG report (2003)	2 <sup>nd</sup> Progress report (2004)
To develop and reinforce the system of scientific advice and to increase the level of expertise of the European Agency for the Evaluation of Medicinal Products (EMA), which would also help to revise and develop European guidelines on the quality, safety and efficacy aspects of biotechnological medicinal products.	<p>1) A joint working of industry and the EMA's CPMP for development of guidance on criteria for new biomarkers / surrogate clinical end-points, which could streamline and accelerate product development.</p> <p>2) The maintenance of the centralised procedure to ensure a uniform treatment of bio(techno)logical medicinal products in Europe, whereby authorisation should remain based on scientific assessment only (quality, safety and efficacy) without any economic consideration, so that faster access to medicines could be achieved.</p>	The review of the pharmaceutical legislation was adopted on 11 March 2004, including a series of provisions for the development and reinforcement of the system of giving scientific advice in EMA.
To introduce an accelerated procedure for assessment and authorisation of products with a major public health interest, and a procedure allowing a conditional access to market of products with a major public health authorisation, for which certain studies are still in progress during the finalisation of the studies.	To introduce unambiguous and explicit reference in pharmaceutical legislation to therapies for severe unmet medical needs and for which fast track and exceptional circumstance provisions will grant faster patient access.	Introduction of a fast-track marketing authorisation for products with a major public health interest, and a conditional marketing authorisation in revised pharmaceutical legislation.
	To introduce separate market authorisation legislation for novel healthcare biotechnology applications, which do not fit existing definitions, e.g. human cell and tissue based products that are neither medicines nor devices.	Legislation will be prepared to harmonise the authorisation procedures for marketing of products/processes from human tissue engineering and presented to the Parliament and the Council before summer 2004.
	To introduce specific regulatory support measures and adaptation of EMA fees for SMEs.	

## **2.2 Regulatory developments and implementation activities**

### 2.2.1 Review of pharmaceutical legislation

In order to take account of scientific and technical progress, the detailed requirements of Annex I to Directive 2001/83/EC on the Community code relating to medicinal products for human use needed adaptation. On 25 June 2003 this led to Commission Directive 2003/63/EC amending Directive 2001/83/EC. Moreover, also because of the experience acquired as a result of the six years operation of marketing authorisation procedures laid down in Regulation (EEC) No 2309/93 and in other Community legislation, the Council adopted a package of Community legislation on pharmaceuticals further updating existing rules. The revised legislation is particularly aimed at 1) responding to innovations, such as the development of new, i.e. biotechnology-derived, substances and gene and cell therapies; 2) enhancing the competitiveness of Europe's pharmaceutical industry, particularly small and medium-sized enterprises in the context of globalisation; 3) ensuring the proper operation of the internal market, in particular in view of the EU's enlargement on 1 May 2004, and; 4) simplifying authorisation procedures and improving transparency. On 31 March 2004 the following texts were adopted:

- Directive 2004/27/EC on the Community code relating to medicinal products for human use (amending Directive 2001/83/EC).
- Directive 2004/28/EC on the Community code relating to medicinal products for veterinary use (amending Directive 2001/82/EC).
- Regulation (EC) No. 726/2004 on authorisation and supervision of medicinal products for human and veterinary use and on the European Medicines Agency (replacing Regulation No. 2309/03).
- Directive 2004/24/EC on traditional herbal medicinal products (amending Directive 2001/83/EC).

The revised legislation reinforces the strengths of the European Medicines Evaluation Agency (EMA) and the centralised authorisation procedure for pharmaceuticals, which has been in place since 1995. While the centralised procedure must now be used for authorisation of biotechnology products, it will be further opened to include more types of new medicines. The revised legislation further includes a 'fast-track' procedure for products of significant therapeutic interest, allowing these products to be assessed and authorised in an expedited way, which mirrors a similar possibility existing in the US market. Also the possibility of a conditional market authorisation has been introduced. This allows for a one-year authorisation, provided that there is an important expected health benefit for the patients and that the company agrees to carry out additional monitoring and clinical studies, which will be reviewed at the end of this period. The revised legislation also provides for an overall increase in transparency and improved access to the results of the decision making process, including assessment reports and the summaries of product characteristics. In addition, for 'copies' of biological products, a definition of these products, so-called 'bio-similar' medicinal product, is introduced. Finally, the revised legislation also includes measures to accelerate the Commission's

decision making process, so that the period between the scientific assessment and marketing of a product is shortened.

### 2.2.2 The European Medicines Evaluation Agency (EMA)

For the implementation (of Part II) of Annex I of Directive 2001/83/EC the EMA issued in December 2003:

- A guideline on comparability of medicinal products containing biotechnology-derived proteins as active substance: quality issues, for which the date of coming into operation is December 2003 (EMA/CPMP/BWP/3207/00/Rev 1\*).
- A guideline on comparability of medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, for which the date of coming into operation is June 2004 (EMA/CPMP/3097/02/Final).

Furthermore, the report of the EMA's Committee on Proprietary Medicinal Products (CPMP) Gene Therapy Group Meeting of February 2004 pointed at differences at national level in regulatory approaches to the environmental risk assessment (ERA) of gene therapy products clinical trials. Many of the gene therapy products currently under development are genetically modified viruses and, as such, these products are classified as GMOs. Within the EU, the construction, production and use of GMOs fall either under Directive 90/219/EEC on the contained use of genetically modified micro-organisms, as amended by Directive 98/81/EC, or under Directive 2001/18/EC on the deliberate release into the environment of GMOs. Although the group had no remit to discuss the implementation of these two directives within EU Member States, it was agreed that it would be useful to discuss, within the context of existing legislation, what scientific information for an ERA should be generated during development. The report further indicated that market authorisation of gene therapy products under Directive 2003/63/EC requires an ERA to be made for the GMO, which should meet the demands of Directive 2001/18/EC. Since there was concern that there could be a lack of consensus amongst Member States on an ERA or on the provision of scientific advice, it was suggested to establish common requirements. In particular with a view to gene therapy products clinical trials at multiple centres in different Member States, there is a need for harmonisation of regulatory approaches to the ERA of gene therapy product clinical trials throughout the EU. A further concern was the availability of environmental data to the public, which might be in conflict with the confidential status of application dossiers for (biotechnological) medicinal products. While guidance on public access is provided within Commission Decision 2002/623/EC, much of it is targeted at agricultural GMOs and not human medicinal products. Therefore it was considered useful to update a specific guidance documents addressing GMOs for human use issued in 1994.

In 2003 the EMA organised a meeting on the 'shortfall of applications' for new medicines. Following this meeting the Commission's Enterprise Directorate-General wrote the European Association for Bioindustries (EuropaBio), asking for practical proposals, which could translate a number of ideas about the regulatory framework into practice, like more transparency, increased collaboration with the US Food and Drug Administration, upstream dialogue with regulators, and SME participation. As a result,

EuropaBio issued, in October 2003, a detailed 10-page proposal with a long series of technical and procedural recommendations to improve regulatory approval for and access to biotech medicinal products in the EU.<sup>5</sup> Compared to the CBAG recommendations of 2003 on regulatory issues to be addressed in the area of healthcare biotechnology, this 10-page proposal by EuropaBio was an extensively elaborated version with specific and detailed suggestions.

Many of these suggestions were taken into account by the EMEA/CPMP Biotechnology Working Party Programme 2004 – 2005. This programme provides a detailed action plan for maintenance, update, revision or development of several guidelines or recommendations on 1) the production of biotechnological and biological medicinal products; 2) vaccines; 3) gene therapy and cell therapy, and; 4) post-authorisation issues. In addition, contributions will be made to the development of a procedure for handling Market Assessment Authorisations (MAAs) in centralised procedures for human medicines consisting of or containing GMOs, while scientific input for the development of procedures and guidance on human tissue engineered and related products will be given. Also the EMEA's discussion paper of 23 March 2004 (EMEA/H/34163/03/Rev 2.0), proposing a Road Map for the agency to 2010, took many recommendations from EuropaBio into account. Key aspects included centralised authorisation procedures, the need for environmental risk assessment for all medicines authorised, the increased scientific competence of the EMEA, enhanced transparency obligations and the reinforcement of risk benefit analysis in ensuring the safety of medicines authorised in the EU. Following the publication of the Road Map to 2010, an information day was organised by the EMEA in June 2004 as an opportunity for interested parties to provide input into the final document, which is now in preparation (EMEA/V/17408/04).

Generally, EuropaBio therefore considers these initiatives by the EMEA as a big move into the right direction. Although there are still several technical and procedural issues to be worked out, so as to ensure a smooth functioning of the reviewed pharmaceutical legislation, industry has confidence in the actions initiated and planned by the EMEA.

### 2.2.3 Legislative proposals for Tissue Engineered Products

On 7 April 2004 Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissue came into force. Human tissues and cells to be used for industrially manufactured products, including medical devices, should be covered by this Directive only as far as donation, procurement and testing are concerned, where processing, preservation, storage and distribution are regulated by other Community legislation. The further manufacturing steps are covered by Directive 2001/83/EC. The scope of Directive 2004/23/EC includes tissues and cells including haematopoietic peripheral blood, umbilical-cord (blood) and bone-marrow stem cells, reproductive cells (egg cells, sperm cells), foetal tissues and cells and embryonic stem cells. Blood and blood products (other than haematopoietic progenitor cells) and human organs, as organs, tissues or cells of animal origin do not fall within the scope of this Directive.

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<sup>5</sup> See [www.europabio.org](http://www.europabio.org)

Moreover, on 6 April 2004 the Commission DG Enterprise published a public consultation proposal for a harmonised Regulation on human tissue engineered products (hTEP) in Europe. The efforts to develop a hTEP Regulation instead of a Directive were welcomed by EuropaBio. But EuropaBio also pointed at a need to clarify the definition of hTEP. It was therefore argued that differentiation should be made between hTEP and Medicinal Products, including Gene Transfer Medicinal Products and Human Somatic Cell Therapy Medicinal Products, as defined in Directive 2001/83/EC (as amended by Directive 2003/63/EC) and Medical Devices.<sup>6</sup> Industry is further concerned about the differentiation of regulatory procedures for allogeneic hTEP (central via the EMEA) and autologous hTEP (via a national authority), a two-tier approach for approval of hTEP, allowing for dispersion of already expertise and less transparency, and the lack of specifically adapted clinical trial guidelines for hTEP. In addition, there is concern that the Regulation on hTEP would only cover viable cells and tissues. If non-viable cells and tissues cannot be included, industry proposed to regulate them by amending the Medical Devices Directive 93/42/EEC. On the other hand, industry appreciated that xenogeneic TEP is excluded from the scope of the Regulation with the provision that the inclusion of xenogeneic tissues into the scope will be re-assessed at a later date. Though, it should also be noted that in parallel to the legislative proposal the EMEA CPMP issued a guidance document “Points to consider on xenogeneic cell therapy medicinal products” in 17 December 2003, for which the date of coming into operation is June 2004.

### **2.3 Main findings and regulatory issues to be further addressed**

- In view of the Commission’s Strategy of 2002, its second progress report and this review, the CBAG’s recommendations of 2003 on regulatory issues in healthcare biotechnology have now largely been addressed by an extensive revision of the Community pharmaceutical legislation. The revised legislation adopted in March 2004 introduces a centralised assessment and authorisation procedure for healthcare biotechnology products, including measures to accelerate the Commission’s decision making process. It also includes a fast-track procedure for products of significant therapeutic interest, allowing their assessment and authorisation in an expedited way, which mirrors a similar possibility existing in the US, while also the possibility of a conditional, one-year market authorisation has been introduced.
- While the revised pharmaceutical legislation reinforces the strengths of the EMEA and the centralised authorisation procedure, the EMEA CPMP has in the mean time adopted two (implementing) technical guidelines for the assessment of biotechnology-derived medicinal proteins. In addition, the EMEA CPMP spelled out a detailed working programme 2004 - 2005 for the maintenance, revision, update and/or development of a series of technical guidelines or recommendations on (the production of) bio(techno)logical medicinal products, vaccines, gene and cell therapy and post-authorisation issues. Also the agency’s Road Map to 2010 proposes a series of implementation activities, in order to further address technical and procedural

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<sup>6</sup> EuropaBio comments to Consultation Paper for hTEP Regulation – April 2004.

requirements for centralised assessment and authorisation procedures and the need for environmental risk assessment (ERA) for all medicines and the need to enhance its transparency obligations. These initiatives by the EMEA are generally appreciated by industry, also because the EMEA provided many opportunities to comment on drafts and proposals. While there remains a series of procedural and technical issues to be resolved, industry has confidence in the actions planned by the EMEA.

- The EMEA noted national differences in regulatory approaches to the ERA of gene therapy products clinical trials. Since many of the gene therapy products currently under development are GM viruses, these products are classified as GMOs, which are either regulated under the contained use Directive 90/219/EEC or the deliberate release Directive 2001/18/EC. Although it had no remit to discuss the implementation of these Directives at national level, it was agreed to discuss the scientific (data) requirements for an ERA. Moreover market authorisation of gene therapy products under Directive 2003/63/EC also requires an ERA to be made for the GMO, which should meet the demands of Directive 2001/18/EC. Since there was concern that there could be a lack of consensus amongst Member States on an ERA or on the provision of scientific advice, it was suggested to establish common requirements. While the EMEA has thus agreed to develop common scientific requirements for an ERA of gene therapy products, there is still a need for harmonisation of regulatory approaches to the ERA of gene therapy products clinical trials throughout the EU, in particular with a view to trials at multiple clinical centres in different EU countries. Meanwhile, for gene therapy trials in multiple centres in different Member States, an approach could be that one of the Member States takes the lead in co-ordinating and fine-tuning the set of the protocol requirements that are to be met by the applicant in to obtain from all involved Member States.
- The placing on the market of human tissue engineered products (hTEP) is not yet covered by Community-wide legislation. In April 2004 the Commission published a public consultation proposal for a harmonised Regulation. Industry generally welcomed the effort to develop a Regulation instead of a Directive. But it also raised many comments concerning the definition of hTEP, the differentiation between national authorisation procedures for autologous hTEP and a centralised authorisation procedure for allogeneic hTEP, and the lack of specifically adapted clinical trial guidelines for hTEP. Xenogeneic TEP were excluded from the scope of the draft Regulation with the provision that the inclusion of xenogeneic tissues into the scope will be re-assessed at a later date. While this exclusion of xTEP from the draft Regulation was appreciated by industry, the EMEA CPMP already issued guidance for the assessment of xenogeneic cell therapy medicinal products. Given this state of affairs, there is a need to speed up the legislative process for the adoption and implementation of a regulatory framework for hTEP, as well as xTEP.

### 3. GMO LEGISLATION AND AGRO-FOOD BIOTECHNOLOGY

#### 3.1 State of affairs according to the three key documents

The table below summarises and compares Action 19 to 23 of the Commission's Strategy Action Plan of 2002, the recommendations of 2003 by the CBAG for adaptation of the regulatory framework for agro-food biotechnology applications and the progress made according to Commission's second progress report.

Action plan (2002)	CBAG report (2003)	2 <sup>nd</sup> Progress report (2004)
Adoption of proposals for Regulations on GM Food and Feed and on Traceability and Labelling.	Member States must implement the deliberate release Directive 2001/18/EC, Regulation (EC) No 1829/2003 on GM food and Feed and Regulation (EC) No 1830/2003 on Traceability and Labelling of GM food and feed.	Directive 2001/18/EC has been fully applicable since 17 October 2002, while only seven Member States have implemented the Directive. Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003 have been fully applicable since April 2004.
Finalisation of legislation for environmental liability, implementation of the Cartagena biosafety protocol and GM plant propagating material.	Urgent completion of legislation that sets in place practicable thresholds for the adventitious presence of EU approved GM seed in non-GM seed.	Regulation (EC) No 1946/2003 on transboundary movement of GMOs has been applicable since 25 November 2003 and aligns the EU's regulatory framework on GMOs, in particular as regards exports, with the Cartagena biosafety protocol.
Adoption of implementing measures, including guidance for detection and sampling and establishment of a publicly accessible molecular register with information on events of genetic modification.	<p>Legislation must be properly transposed into national law, and properly and consistently enforced.</p> <p>The large backlog of submissions resulting from five years of a de facto moratorium on approvals must be dealt with quickly. Products assessed safe must be approved, so that they may be offered to the market.</p> <p>Prohibitions by Member States on already approved GMOs must be withdrawn, where the scientific committees have indicated that there is no 'new' information relating to risk.</p>	<p>Member States must transpose and implement Directive 2001/18/EC and withdraw national measures invoked earlier.</p> <p>A number of implementing measures for Directive 2001/18/EC, Regulation (EC) No 1829/2003 on GM food and Feed and Regulation (EC) No 1830/2003 have been adopted or are in preparation, including adoption of labelling thresholds for the adventitious presence of authorised GM seed in non-GM seed under Directive 2001/18/EC.</p>
Report on feasibility of options to improve further consistency and efficiency of the framework for authorising GMOs for deliberate release into the environment.		

<b>Action plan (2002)</b>	<b>CBAG report (2003)</b>	<b>2<sup>nd</sup> Progress report (2004)</b>
Support development of methods for monitoring long-term environmental impacts of GMOs and for monitoring effects of GM food and feed.		
	<p>EU approved products should not arbitrarily prohibited by national or regional law from being offered to the market in certain Member States or regions.</p> <p>The labelling threshold of 0.9% must be recognised as the guiding baseline in establishing coexistence of GM crops with conventional or biological crops.</p> <p>Those wishing to offer produce guaranteed to be lower than the legally binding threshold must themselves be responsible for additional measures.</p>	<p>On 23 July 2003 the Commission adopted a Recommendation setting out guidelines for national strategies and best practices to ensure coexistence of GMOs with conventional and organic farming. The subsidiarity approach was endorsed by the Council and the Parliament in July 2003, when Article 26(a) of Directive 2001/18/EC was introduced, which allows Member States to take measures to avoid the unintended presence of GMOs in other products. On 29 September 2003 the Council of Agricultural Ministers was split between supporting the subsidiarity approach and demanding coexistence rules at the Community level.</p>
		<p>For authorisation to place any GM variety of animal species on the market the existing regulatory framework for GMOs appears to be satisfactory at the Community level. Introduction of products obtained from cloned livestock into the food chain may raise ethical, social and safety concerns. Initiatives will be launched on the potential benefits, risks and new policy issues associated with the application of animal cloning.</p>
	<p>Introduction of a transparent approval system for GMO-derived food enzymes.</p> <p>Clarification of the scope of Regulation (EC) No 1829/2003 concerning GM micro-organisms no longer present in the final product. Guidance from the Commission on Directive 90/219/EEC considering 'self-cloned' micro-organisms as GMMs.</p>	

## **3.2 Regulatory developments and implementation activities**

### 3.2.1 The EU regulatory framework for GMOs

While the deliberate release Directive 2001/18/EC (repealing Directive 90/220/EEC) came into force on 17 October 2002, Regulation (EC) No 1829/2003 on GM Food and Feed and Regulation (EC) No 1830/2003 on Traceability and Labelling of GM Food and Feed became fully applicable as of 18 April 2004. The following measures have so far been adopted for implementing this EU regulatory framework for the development and use of GMOs ‘from farm to fork’:

- Council Decision 2002/83/EC of 3 October 2002 establishing, pursuant to Directive 2001/18/EC, the summary notification information format for notification of Part B releases.
- Commission Decision 2003/701/EC of 29 September 2003 establishing, pursuant to Directive 2001/18/EC, a format for presenting the results of Part B releases of GM higher plants.
- Council Decision 2002/811/EC of 3 October 2002 establishing guidance notes supplementing Annex VII to Directive 2001/18/EC (for Part C releases).
- Council Decision 2002/812/EC of 3 October 2002 establishing, pursuant to Directive 2001/18/EC, the summary information format relating to the placing of the market of GMOs as or in products.
- Commission Decision 2004/204/EC of 23 February 2004 laying down detailed arrangements for the operation of the registers for recording information on genetic modifications in GMOs.
- Commission Decision 2002/623/EC of 24 July 2002 establishing guidance notes supplementing Annex II of Directive 2001/18/EC.
- Commission Regulation (EC) No 65/2004 of 14 January 2004 establishing, in relation to Regulation (EC) No 1830/2003, a system for the development and assignment of unique identifiers for GMOs.
- Commission Regulation (EC) No 641/2004 of 6 April 2004 as regards the application for the authorisation of new GM food and feed, the notification of existing products and adventitious or technically unavoidable presence of GM material which has benefited from a favourable risk evaluation.

In addition, since 25 November 2003 Regulation (EC) No 1946/2003 on transboundary movement of GMOs has been applicable and aligns the EU’s regulatory framework on GMOs, in particular as regards exports, with the Cartagena biosafety protocol. In this context, the Commission’s (Decision on a) system of unique identifiers of GMOs also aligns the consensus reached at the First Meetings of the Parties to the Cartagena Protocol of February 2004 as regards documentation requirements for the transboundary movement of GMOs. In addition, this Commission Decision is an implementing measure for Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003, as well as Directive 2001/18/EC.

Furthermore, Directive 2004/35/EC on environmental liability with regard to the prevention and remedying of environmental damage was adopted in April 2004. Within this scope, a regime of strict liability is foreseen for environmental damage from GMOs, i.e. there is no requirement to demonstrate negligence or criminal damage. The Directive foresees that in situation where an operator can demonstrate that the damage in question was the result of emissions or events explicitly authorised or where the potential for damage could not have been known when the emission or event took place, Member States may allow the operator not to bear the costs of remedial actions. The Directive specifically excludes civil liability for property damage or economic loss from, for example, adventitious presence of unwanted GM material/traits/species from neighbouring properties in crops or wild relatives.

In addition, the Commission is also in the process of drafting a proposal for establishing threshold levels for seeds, where adventitious or technically unavoidable traces of authorised GMOs cannot be excluded, in accordance with Article 21.2 of Directive 2001/18/EC. Identical thresholds will then be adopted under the seed and other plant propagating material legislation.

### 3.2.2 Directive 2001/18/EC

On 31 August 2004 the Commission issued its report on the experience of Member States with GMOs placed on the market under Directive 2001/18/EC and incorporating a specific report on the operation of Parts B and C of the Directive.<sup>7</sup> According to this report, seven of the EU 15 Member States and eight of the acceding countries have communicated transposition measures. Eight of the EU 15 Member States have been taken by the Commission to court for non-transposition.

The Commission further reported that since the adoption of Directive 2001/18/EC a slight increase in the number of Part B notifications, mostly field trials with GM plants, has occurred in France, Germany, Spain and the UK. In all other countries there has been a reduction or no change in the number of Part B notifications. Moreover, between January 2003 and March 2004 twenty-four Part C applications (for placing on the market) were submitted. A number of these applications had originally been submitted under Directive 90/220/EEC (prior to 17 October 2002) and were complemented under Directive 2001/18/EC in accordance with Article 35. These applications are now at various stages of the authorisation process. Although Part C of Directive 2001/18/EC covers all commercial releases, Regulation (EC) No 1829/2003 now defines procedures for placing GM food and feed, including GM crops for food and feed use, on the market. When the new Regulation became applicable as of 18 April 2004, Part C notifications submitted under Directive 2001/18/EC, concerning products for which feed use was included and for which an assessment report had not yet been provided, were to be transformed into applications under the new Regulation (EC) No 1829/2003. Likewise, requests submitted under the novel food Regulation (EC) No 258/97, for which the initial assessment report

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<sup>7</sup> Report from the Commission to the Council and the European Parliament on the on the experience of Member States with GMOs placed on the market under Directive 2001/18/EC and incorporating a specific report on the operation of parts B and C of the Directive, COM(2004)575 final, 31.08.04.

had not been forwarded or for which an additional assessment report had been requested, were to be transformed into applications under the new Regulation. Since applications for GMOs for food and feed use will be authorised under this Regulation, the number of Part C applications under Directive 2001/18/EC may be reduced in the future as a consequence of the evolving legislative framework.

Under Directive 90/220/EEC, nine Article 16 cases were invoked by Austria, France, Luxembourg, Germany, UK and Greece to provisionally ban or restrict the placing on the market of GMOs approved under that Directive. In December 2003 the Commission requested to consider their pending safeguard clauses and, if necessary, to re-submit them under Article 23 of Directive 2001/18/EC. So far Austria and Greece have submitted new evidence, which has been forwarded by the Commission to the European Food Safety Authority (EFSA) for a scientific opinion. The Commission will take a Decision on the matter on the basis of this opinion.

The Commission further reported that additional working groups of Member States Competent Authorities (CAs), chaired by the Commission, have been established to address specific issues, like herbicide resistance, Bt toxins, antibiotic resistance markers (ARMs), post-marketing monitoring and ease of access and exchange of information. The Working Group on ARMs will thereby use the opinion delivered by the EFSA on 2 April 2004. Moreover, the CAs have arrived at a common understanding on the implementation of specific articles of the Directive as a result of the regular exchange of views among CAs.

Compared to Directive 90/220/EEC the requirements for the environmental risk assessment (ERA), Directive 2001/18/EC stipulates stricter requirements for the ERA, for which Commission Decision 2002/623/EC is an implementing measure providing guidance. In practice some Member States already imposed stricter requirements than necessary under Directive 90/220/EEC. In these cases Directive 2001/18/EC has not led to significant changes. Other Member States however had to increase their requirements, particularly in relation to indirect and delayed effects. On the one hand, this suggests that the Directive has or will lead to a greater degree of harmonisation. On the other hand, there is insufficient experience at this stage to assess the degree of consistency among Member States with regard to the requirements of the ERA.

According the Commission's report, current authorisation process in terms of forms and guidance is focused on GM plants. In this field the Commission suggests that as follow-up to previous EC-sponsored research on safety of GMOs further research should be encouraged on: 1) rates of gene flow and introgression in relation to the adventitious presence of GMOs in (non-GM) seeds, food and feed; 2) the efficacy of measures to limit pollen flow, and; 3) the environmental impact of different methods of conventional farming against which to compare the findings from GM crop growing.

The Commission further pointed out that it will also be necessary to develop specific guidance on the risk assessment of non-plant GMOs, as GM medicines and GM animals are also under development and their authorisation will require consideration of different

issues. With a view to GMOs for medical use, which are excluded from Part C applications according to Directive 2001/18/EC, Article 12.2, some industry stakeholders requested further guidance on the interaction between different pieces of legislation. Based on their experience for Part B applications they believe that it may be necessary to submit market applications for GMOs for medical use under both Directive 2001/18/EC and the medical authorisation procedures.

Generally, industry stakeholders advocated a centralised Community authorisation procedure. The experience of Member States CAs with the centralised procedure for the authorisation of medicinal products under Regulation (EEC) No. 2309/93 suggests that there is a need to clarify the obligations of the EMEA, when consulting Member States CAs, particularly with regard to the environmental risk assessment (ERA).<sup>8</sup> Experience has also shown that, for the purpose of cultivation of GM plants, Member States were not ready to accept the ERA carried out by other Member States, even of a common basis for risks is foreseen in the Directive. Since as of 18 April 2004 Regulation (EC) No 1829/2003 provides a centralised procedure with the European Food Safety Authority (EFSA), the Commission will consider the need for a centralised procedure under Directive 2001/18/EC in the light of experience acquired in the implementation of the Regulation.

Compared to Directive 90/220/EEC the requirements for public consultation on Part B and Part C applications under Directive 2001/18/EC are stricter. For Part B application Member States shall lay down own arrangements (on the basis of subsidiarity), which should allow the public or groups to express an opinion during a reasonable time-period. These time periods vary between 21 to 60 days among Member States. For Part C applications the Directive requires the Commission to make the summary of notification and the assessment report publicly accessible and foresees a period of thirty days for public consultation on each. Given the recent nature of mandatory public consultation, some public interest groups and individuals have experienced difficulties in finding information and have raised concern that the information made available may not be sufficient to develop an opinion. There are also concerns about how public responses are taken into account in the decision-making process, in particular, responses based on socio-economic and ethical factors, given the Directive's focus on scientific assessment of applications.

According to the Commission's report, many industry stakeholders consider the ERA and public information requirements under Directive 2001/18/EC a regulatory burden, which substantially increases research and development costs. This would make it more difficult for small companies and public research institutions to bring products to the market. In particular, the requirement to provide location details of field trials causes concern in the light of experience acquired with malicious destruction of these field trials in various Member States. Though, it should also be noted that the Directive leaves it to the Member States how to implement the public information and consultation requirements for Part B field trials at national level. As a consequence, there are national differences. For example, while in a few Member States the applicant is required to place an

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<sup>8</sup> See also paragraph 2.2.

announcement in a (national and/or local) newspaper, in other Member States the national public authority has taken the responsibility for placing an announcement in one or more (national and/or local) newspaper.<sup>9</sup> Also the level of detail of information about the locations of field trials, which is publicly disclosed, seems to vary at national level. Against this background, it could be useful for the Commission and the Member States to monitor the implementation of the ERA and public information and consultation requirements at national level, including the division of (in)direct costs involved, and (to continue) to exchange information about best practices for public information and consultation at national level.

### 3.2.3 Coexistence of GMOs with conventional and organic farming

According to the Commission's report, all deliberate releases of GMOs into the environment raise issues of coexistence. Regulation (EC) No 1829/2003 has introduced an amendment to Directive 2001/18/EC (new Article 26a). This article refers to possible national measures to avoid the unintended presence of GMOs in other products, as well as to Commission guidelines on coexistence, for which a Recommendation was published on 23 July 2003. One of the measures suggested by the Recommendation is that the register established in accordance with Article 31.1(b) of Directive 2001/18/EC could be a useful instrument to monitor developments of GM crops and to help farmer co-ordinate local production patterns and monitor developments concerning the different types of crops. The Recommendation further points out that under Directive 2001/18/EC there is a legal requirement for farmers, who cultivate GM crops, to have systems for traceability and labelling in place. Since the Recommendation also notes that the type of national instruments adopted might have an impact on the application of national liability rules in the event of economic damage resulting from admixture, Member States were advised to examine their civil liability laws and, in this context, they might want to explore the feasibility and usefulness of adapting existing insurance schemes or setting up new schemes.

So far some Member States adopted national coexistence measures. The first type of measures notified to the Commission aimed at either setting up GMO-free regions or a limiting (as much as possible) cultivation of GMOs by setting strict measures at national/regional level. Such blanket policy would however not be acceptable when seeking to impose conditions that could not be justified in terms of protection of human health and the environment. Other Member States are also considering their policies on coexistence, while in Denmark and Germany national strategies are in advanced state of adoption. Furthermore, in December 2003 the Commission recognised for the first time that the main coexistence principles laid down in its Recommendation, had been taken into account in a notification, even though additional conditions were requested before this was found acceptable by the Commission.

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<sup>9</sup> SBC, Means to improve the consistency and efficiency of the legislative framework in the field of biotechnology, study contract number B4-3040/2003/359058/MAR/C4, carried out by Schenkelaars Biotechnology Consultancy (SBC), NL, in co-operation with Risk and Policy Analysts Ltd, UK, on behalf of the European Commission, April 2004; this study provided the basis for the Commission's report on Directive 2001/18/EC (see note 7.)

The Commission Recommendation was also discussed in the Council of Agricultural Ministers of 29 September 2003, where there appeared to be a split between supporting the subsidiarity approach and requesting rules at the Community level. Furthermore, in December 2003 the European Parliament adopted an own-initiative report calling for uniform and binding Community rules, including Community-wide liability rules and insurance in respect of possible economic damage in connection with coexistence.

While so far a number of draft coexistence measures have been notified to the Commission, the Commission is also aware of non-notified coexistence measures, taken at national, regional or local level. These measures might contradict Community legislation and could therefore prompt infringement procedures by the Commission.

In its second progress report of 2004 the Commission therefore suggested Member States to ensure an exchange of information on successful approaches and best practices and to notify national or regional measures on co-existence to the Commission. The Commission on its turn would enhance its co-ordination role as foreseen by Directive 2001/18/EC, in order to smooth any potential problems linked to the development of co-existence strategies by Member States. The Commission would also report to the Council and the European Parliament, using information from the Member States, including, where appropriate, an evaluation and assessment of all possible and necessary steps to be taken.

At the meeting of the Council of Agriculture Ministers of 18 October 2004, some 13 Member States gave their support to a joint Danish-Italian request to set up a European task force to ensure the co-existence of GM crops and other crops. These Member States all agreed on the need to collect and disseminate information at the EU level. They also agreed on the need to identify research requirements concerning co-existence at pan-European level, pointing to the need to set values for the minimum labelling thresholds levels of (EU-authorized) GM seeds in lots of non-GM seeds.

#### 3.2.4 Community seeds legislation

In October 2003 the Commission reported that it was examining the issue of post-marketing monitoring plans for twenty-three GM maize varieties inscribed in national catalogues of France, Spain and the Netherlands, which were awaiting inscription into the Common Catalogue of agricultural species in accordance with Directive 2002/53/EC.<sup>10</sup> According to that Directive, the Commission is required to inscribe in the Common Catalogue any varieties, which have been added to national catalogues. The GMO ('event'), on which the variety is based, must be authorised under Directive 2001/18/EC for its use in cultivation and the GM material must be authorised under either the Novel Food Regulation (EC) 258/97 or the GM food and feed Regulation (EC) No 1829/2003.

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<sup>10</sup> CEC, Commission Staff Working Document: Information note concerning forthcoming decision on GMOs, and GM food, feed and seed, SEC(2003) 1131, Brussel, 13.10.2003.

On 8 September 2004 it was the first time the Commission approved inscription of GM plant varieties in the Common Catalogue. In total seventeen GM maize varieties based on 'event' MON810, which has been approved in the EU since 1998, were inscribed.<sup>11</sup>

On the same day the Commission also indicated in a brief statement that it had postponed the decision to be made on the draft Commission Decision for establishing minimum threshold levels for adventitious or technically unavoidable traces of GM seeds in other products.

### 3.2.5 Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003

In October 2003 the Commission reported it was preparing implementing measures and guidance for Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003, in order to ensure full applicability by April 2004.

On 16 January 2004 Commission Regulation (EC) No 65/2004 was published, which established a system for the development of unique identifiers for GMOs. In addition, the Commission presented a draft Commission Regulation (SANCO/2004/385) at the 1<sup>st</sup> meeting of Standing Committee on the Food Chain and Animal Health (SCFCAH). The purpose is to provide rules for the preparation and presentation of applications for authorisation, the notification of existing products and the application of the 0.5 % threshold for the adventitious presence of GM material.<sup>12</sup> Member States welcomed the draft and did not express any major concerns only technical comments. A number of drafting changes was agreed upon, resulting, on 6 April 2004, in adoption of Commission Regulation (EC) No 641/2004 as regards the application for the authorisation of new GM food and feed, the notification of existing products and adventitious or technically unavoidable presence of GM material which has benefited from a favourable risk evaluation.

Yet, at the first meeting of SCFCAH concerns were also expressed on the implementation of the labelling rules, which are not subject of the Commission Regulation, in particular as regards the application of the 0.9 % threshold. Further to questions raised by some Member States on the application of Regulation (EC) No 1829/2003, the proposal was to organise a meeting of a working group. Furthermore, the Commission presented a draft Commission Recommendation on technical guidance on sampling and testing to Member States, as foreseen by Article 9(2) of Regulation (EC) No 1830/2003. Since there were many comments and remarks, Member States were invited to take into account the views of their CAs for Directive 2001/18/EC, which will deliver an opinion to the Commission on this draft. At the 2<sup>nd</sup> meeting of the SCFCAH of 23 June 2004 the exchange of views between Member States continued.<sup>13</sup> Issues discussed included fermentation products, self-cloning and operation of the 0.9 % threshold, the draft Commission

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<sup>11</sup> European Commission, Press Release, IP/04/1083.

<sup>12</sup> Short Summary of the 1<sup>st</sup> meeting of the Standing Committee on the Food Chain and Animal Health on 10 February 2004.

<sup>13</sup> Agenda of the 2<sup>nd</sup> meeting of the meeting of Standing Committee on the Food Chain and Animal Health on 23 June 2004.

Recommendation on technical guidance for sampling and detection, and the contribution of companies to the costs for validation of detection methods.

In the mean time the Community Reference Laboratory (CRL) has already developed a series of guidance documents on the validation of the detection methods, which have to be submitted by the applicants under Article 47 of Regulation (EC) No 1829/2003. Moreover the CRL has also completed the validation of several detection methods of GM crops, which are currently at various stages in the authorisation procedures either under Directive 2001/18/EC or Regulation (EC) No 1829/2003.

So far, seventeen GM crops ('events') have been authorised for food used in the EU either under Directive 90/220/EEC or the novel food Regulation (EC) No 258/97. Eight of these GM crops, plus one other GM crop, have also been authorised for feed use under Directive 90/220/EEC. Moreover, three applications under Regulation (EC) No 258/97 and three applications under Regulation (EC) No 1829/2003 are currently pending for food use and there are twenty applications pending for feed use. Eleven of these applications, which were submitted under either the old or new deliberate release Directive, required a transformation into an application under Regulation (EC) No 1829/2003/EC.

#### 3.2.6 The European Food Safety Authority (EFSA)

From July 2003 to July 2004 the EFSA Scientific Panel on GMOs delivered ten opinions. Three of these opinions concerned requests from the Commissions in relation to the invocation by Member States of the safeguard clause under either the old or new deliberate release Directive. Five opinions were delivered on notifications of GM crops under either one of the deliberate release Directives or Regulation (EC) No 1829/2003.

One of the other two opinions concerned guidance on the use of antibiotic resistance markers (ARMs) in GM plants. This opinion of 2 April 2004 will also form the basis for the development of clear and transparent criteria with a view to a common application of Article 4.2 of Directive 2001/18/EC.

Furthermore, since Regulation (EC) No 1829/2003 provides that the EFSA shall publish detailed guidance to assist the applicant in the preparation and presentation of the application for the authorisation under this Regulation or Directive 2001/18/EC, a draft guidance document for the risk assessment of GM plants and derived food and feed was issued on 2 April 2004. Thereby it should be noted that the Regulation leaves the applicant the choice either applying for an authorisation under Part C of Directive 2001/18/EC, or requesting the environmental risk assessment (ERA) to be carried out at the same time as the food and feed safety assessment under the Regulation. However, if the GMOs are seeds or other plant propagating material, the ERA must be delegated by the EFSA to a national Competent Authority (CA) for Directive 2001/18/EC. Interested parties were given the opportunity to comment on the EFSA draft guidance document until 30 April 2004. Subsequently, a stakeholder consultation meeting was organised on 25 May 2004 to discuss the comments received.

The draft guidance document also noted that food additives (Directive 89/107/EEC), flavourings (Directive 88/388/EEC) and feed additives (Regulation (EC) No 1831/2003) containing, or consisting of or produced from GM plants and food and/or feed containing, or consisting of or produced from GMMs (Regulation (EC) No 1829/2003) do not fall within the scope of this draft guidance. For these categories of products parallel guidance documents are in preparation. In addition, guidance will be prepared for the placing on the market of food and/or feed consisting of, containing or produced from GM animals (Regulation (EC) No 1829/2003). Additional guidance also needs to be developed for the ERA of GM plants used to produce medicinal products ('plant-made pharmaceuticals') for human and veterinary use (Regulation (EEC) No 2309/93), as well as other non-food purposes, e.g. 'plant-made industrial compounds' and GM plants for phytoremediation).

### 3.2.7 Industrial biotechnology

The CBAG report of 2003 indicated that Europe is still a frontrunner in industrial biotechnology (IB) research and innovation. But its global competitive position is eroding quickly, due to long-term strategic investments by the USA and East Asia, as well as to Europe's structural weaknesses. Concerning the food enzyme legislation under preparation, industry expects a clear and simple approval system. According to the CBAG, there is also a need for clarification of the scope of the GM food and feed Regulation as to (fermentation) products produced with GM micro-organisms (GMMs) no longer present in the final product. In addition, there is a need for clear Commission guidance as to whether to consider 'self-cloned' micro-organisms as GMOs when implementing the contained use Directive 90/219/EEC.

As a few Member States consider a self-cloned, i.e. homologous recombinant-DNA modified, micro-organism not a GMM/GMO in the meaning of the contained use Directive, a study of 2003 commissioned by the Netherlands Ministry of Economic Affairs also recommended harmonisation, in order to prevent unfair trading practices and fraudulent 'non-GM' labelling claims.<sup>14</sup> In addition, in view to labelling requirements of additives and enzymes derived of GMMs under Regulation (EC) No 1829/2003, the study also identified a need to clarify the distinction between produced 'from' a GMO and produced 'with' a GMO, and whether their 'detectable' presence in food or feed would require labelling.

As regards the safety assessment of (GM) micro-organisms used in feed/food and feed/food production, the Commission issued a working paper, for which the deadline for comments from invited parties was 30 June 2003. The purpose was to explore the possibility of a so-called 'Qualified Presumption of Safety (QPS)' system for the EU, similar in concept and purposed to the so-called definition of Generally Recognised As Safe (GRAS) used in the US. In a similar vein the EFSA opinion of 11 December 2003 addressed guidance notes supplementing Part B of Annex II of Directive 90/219/EEC, as amended by Directive 98/81/EC, on the contained use of GMMs. The EFSA opinion

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<sup>14</sup> Workability Practices (Part II): New and proposed EU legislation for GMOs from farm to fork: Bottlenecks for notifiers and operators and recommendations to authorities, Schenkelaars Biotechnology Consultancy, commissioned by the Netherlands Ministry of Economic Affairs, February 2003.

supports the necessity of defining criteria of individual types of GMMs for human health and the environment and ultimately their suitability for inclusion in Part C of Annex II of the Directive process, whereby they can be excluded from the provisions of the Directive. A self-cloned micro-organism would then no longer be considered a GMM/GMO. As a consequence, food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a self-cloned micro-organism would not fall within the scope of the GM food and feed Regulation and would not have to be labelled.

In September 2004 the Chair of the Standing Committee on the Food Chain and Animal Health (SCFCAH)<sup>15</sup> concluded that, with exception of one Member State disagreeing and one Member State reserving its positions, there was consensus that:

- Food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a GMM, which is not present in the final product, are not included in the scope of the GM food and feed Regulation. These food and feed have to be considered as having produced with the GMM, rather than from the GMM
- Food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a GMM, which is present in the final product, totally or partially, whether alive or not, are included in the scope of the GM food and feed Regulation, in regard of both authorisation and labelling.

Whether this distinction would be workable, controllable and verifiable from a business point of view is however not clear. Moreover, it is also not clear whether other stakeholders, including consumer organisations, agree that this distinction would serve one of the objectives of the GM food and feed Regulation, that is freedom of consumer choice.

According to the record of the SCFCAH meeting of September 2004, the question of the possible extension of the scope of the GM food and feed Regulation to some or all food and feed produced by fermentation using a GMM not present in the final product, as regards their safety assessment, authorisation and labelling will be reviewed in the context of the report to be presented by the Commission in November 2005.

In conclusion, the regulatory uncertainty surrounding fermentation products from industrial biotechnology for food and feed use has not yet been resolved by the Commission and the Member States. Given this state of affairs, the two following options, addressing both issues, e.g. labelling and self-cloning, might be considered:

- Exclude self-cloned GM (GRAS/QPS) micro-organisms from the contained use Directive. As a consequence, food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a self-cloned GM micro-organism do not fall under the GM food and feed Regulation, and therefore there would be no need to label, irrespective of the presence of the self-cloned micro-

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<sup>15</sup> SCFCAH, Summary record of the 3<sup>rd</sup> Meeting – 24 September 2004, Section on genetically modified food and feed and environmental risk.

organism in the final product. From an innovator's point of view, this option would probably address many of their concerns about the workability, controllability and enforceability at once. Other stakeholders, like consumer organisations, might perceive an inconsistency with the labelling requirements for food and feed ingredients derived of GM crops produced by homologous recombinant DNA genetic modification techniques, which could be considered 'self-cloned crops'.

- Harmonise the implementation of the contained use Directive for self-cloned (GRAS/QPS) micro-organisms as GMM/GMO throughout the EU, and foresee labelling of all food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a self-cloned GMM under the GM food and feed Regulation, irrespective of whether the self-cloned GMM is present in the final product. From a consumer point of view, this would be consistent with the labelling requirements for food and feed (ingredients) derived of GM crops, irrespective of the presence of 'modified' DNA or protein in the final product, and would therefore require a similar documentation trail for verification of labelling. Precisely for this reason, innovators will probably consider this option not workable, controllable and enforceable, in particular with a view to imported food and feed (ingredients including additives, flavourings and vitamins) produced by fermentation using a self-cloned (GRAS/QPS) micro-organism.

For the review of the implementation of the GM food and feed Regulation and the traceability and labelling Regulation, on which the Commission must report not later than 7 November 2005, an integrated socio-economic impact assessment, an assessment of the administrative burden to business, an assessment of the regulatory quality and an international benchmarking (see paragraph 4.3) could provide solid insights into the workability, controllability and enforceability of the pros and cons of both options.

### **3.3 Main findings and regulatory issues to be further addressed**

- In view of the Commission's Strategy of 2002, its second progress report and this review, a major part of the CBAG's recommendations of 2003 on regulatory issues in agro-food biotechnology has been addressed. Basically, the EU regulatory framework for the development and use of GMOs from farm to fork now comprises 1) the deliberate release Directive 2001/18/EC; 2) the GM food and feed Regulation (EC) No 1829/2003; 3) the traceability and labelling Regulation (EC) No 1830/2003; 4) the transboundary movement Regulation (EC) No 1946/2003, and; 5) the environmental liability Directive 2004/35/EC.
- Yet, there is one crucial piece of legislation, which still needs to be adopted, that is a Commission Decision for establishing the values of the minimum thresholds for adventitious or technically unavoidable traces of GM seeds in other products under Directive 2001/18/EC, which then need to be adopted under the legislation for seeds and other plant propagating materials.

- At the meeting of the Agriculture Council of 18 October 2004, some 13 Member States gave their support to a joint Danish-Italian request to set up a European task force to ensure the co-existence of GM crops and other crops. These Member States all agreed on the need to collect and disseminate information on successful approaches and best practices on co-existence at the EU level. They also agreed on the need to identify research requirements concerning co-existence at pan-European level, thereby pointing to the need to set values for the minimum labelling thresholds levels of (EU-authorised) GM seeds in lots of non-GM seeds.
- Directive 2001/18/EC has been fully applicable since 17 October 2002 and a series of guidance documents have been adopted for its common implementation. However, it should also be noted that there is currently insufficient experience to assess the degree of consistency among Member States with regard to the requirement of the Environmental Risk Assessment (ERA). Several working groups of Member States Competent Authorities have in the mean time been established to address specific technical issues. In addition, as follow-up to previous EC sponsored GMO-biosafety research, the Commission report on Directive 2001/18/EC suggested that the following areas needed to further research on: 1) rates of gene flow and introgression in relation to the adventitious presence of GMOs in (non-GM) seeds, food and feed; 2) the efficacy of measures to limit pollen flow, and; 3) the environmental impact of different methods of conventional farming against which to compare the findings from GM crop growing.
- So far seven of the EU 15 Member States and eight of the acceding countries have communicated transposition measures to the Commission. Eight of the EU 15 Member States have therefore taken to court for non-transposition. The Commission also started investigating cases where a member state has invoked the safeguard clause to ban or restrict the placing on the market of a GMO authorised in the EU. For three cases the EFSA delivered an opinion upon request from the Commission.
- Generally, industry advocated a centralised Community authorisation procedure. Experience has however shown that, for the purpose of cultivation of GM plants, Member States were not ready to accept the ERA carried out by other Member States, even if a common basis for risks is foreseen in the Directive. Since Regulation (EC) No 1829/2003 provides a centralised procedure with the EFSA, the Commission indicated that the need for a centralised procedure under Directive 2001/18/EC will be considered in the light of experience acquired in the implementation of the Regulation.
- Also the authorisation procedures related to GM crops have been re-started. But in all cases of approval so far under either Directive 2001/18/EC or Regulation (EC) No. 1829/2003, Member States had difficulties finding a common position on the risk assessment (data) requirements in spite of a position opinion by the EFSA, thereby leaving it to the Commission to make the final decision.

- Compared to Directive 90/220/EEC requirements for public information and consultation under Directive 2001/18/EC are stricter. Although in the context of Part C applications for placing on the market some public interest groups and individuals have experienced difficulties in finding information, thereby also expressing concerns about public responses are taken into account in decision making, they appreciated the new requirements. Industry generally considers the ERA and public information requirements under Directive 2001/18/EC a regulatory burden, which substantially increases research and development costs, making it more difficult for small companies and public research institutions to bring products to the market. The requirements to provide locations details of field trials caused particular concern in the light of experience acquired with destruction of field trials in various Member States. Against this background, it could be useful for the Commission and the Member States to monitor the implementation of the ERA and public information and public consultation requirements at national level, including the division of (in)direct costs involved, and (to continue) to exchange information about best practices at national level.
- Both Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003 came fully into force in April 2004. So far, two Commission Regulations (No 65/2004 and No 641/2004) have been adopted as implementing measures. Yet, there are concerns among Member States on the implementation of the 0.9 % labelling-threshold, which is not subject of Regulation No 641/2004. Moreover, a draft Commission Recommendation on technical guidance for sampling and testing has been presented to the Member States but has not yet been adopted because of many comments. In the mean time the Community Reference Laboratory has developed guidance on the validation of detection methods. It has also completed the validation of several detection methods of GM crops, which are currently at various stages in the authorisation procedures either under Directive 2001/18/EC or Regulation (EC) No 1829/2003.
- While the EFSA so far delivered five opinions on notifications of GM crops, currently pending under either one of the deliberate release Directives or Regulation (EC) No 1829/2003, it issued a draft guidance document for the risk assessment of GM crops and derived food and feed on 2 April 2004. Interested parties had the opportunity to submit comments until 30 April 2004 and were invited by the EFSA for a stakeholder consultation on 25 May 2004. The final guidance document is now in preparation. The EFSA further indicated that it is preparing guidance documents for food and feed additives derived of GM crops and for food and feed derived of GM animals. Additional guidance will also be developed by the EFSA for the ERA of GM plants used to produce 'plant-made pharmaceuticals' and GM plants used to produce 'plant-made industrial compounds'.
- In December 2003 the EFSA Scientific Panel on GMOs delivered an opinion, addressing guidance notes supplementing Part B of Annex II of Directive 90/219/EEC, as amended by Directive 98/81/EC, on the contained use of GM micro-organisms (GMMs). In essence, the EFSA supported the development of scientific

criteria for exclusion of self-cloned GM (GRAS/QPS) micro-organism from the contained use Directive. But there is still an urgent need for a scientific follow-up by the EFSA, as it could provide a basis for adopting a common position by the Member States as to whether or not a so-called 'self-cloned' micro-organism should be regarded as a GMM in the meaning of Directive 90/219/EEC. Moreover, there is an urgent need to adopt a common position as to whether food/feed ingredients and enzymes produced by fermentation using a self-cloned GMM fall under (the labelling requirements of) Regulation (EC) No 1829/2003.

## **4. IMPLEMENTATION AND COHERENCE**

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### **4.1 State of affairs according to the four key documents**

#### 4.1.1 The Competitiveness Council Meeting of 17 and 18 May 2004

On 17 and 18 May 2004 the Competitiveness Council held a public debate on issues summarised by the Commissioners for Internal Market, Industry and Research on the basis of recent Commission communications covering aspects of competitiveness and innovation and on approaches to better regulation, including impact assessment of new Community legislation. Pursuant to the debate, the Competitiveness Council adopted a series of conclusions on these aspects. Life sciences and biotechnology were considered by the Council important for the development of a knowledge-based economy, as they were key enabling technologies for future industrial development and innovation. The Council also recognised the importance of effective governance and the need for full commitment of all relevant actors to proactively support evolving actions under the EU Life Sciences and Biotechnology Strategy. With a view to legislation, the Council called on the Commission and the Member States within their respective competencies to:

- Avoid and remove unnecessary regulation and administrative burdens, and to exploit e-government and one-stop shops, having regard to the cumulative impact of legislation.
- Implement by the due date and enforce legislation, which is necessary to create a legally predictable operating environment for business.
- Implement the legislative framework for GMOs and pharmaceuticals now in place.

Moreover, with a view to Community policy on Better Regulation, the Council recalled the Inter-institutional Agreement on Better Lawmaking, and it strongly endorsed the work of the Commission in implementing its Better Regulation Action Plan. The Council also acknowledged that better regulation is a joint responsibility of the European institutions and the Member States. While this concerned all policy areas, better regulation must take account of the economic, social and environmental aspects of sustainable development and required sustained effort over the long-term. The Council therefore invited the Commission and Member States to:

- Consider priority areas and time scales for simplification.
- Continue to further refine the integrated impact assessment procedure, including quantification, alternative policy options, and where possible considering indirect effects, and with a particular emphasis on enhancing the competitiveness dimension.
- Make information relevant to impact assessment available to the public in the context of consultation in order to maximise the benefits of the consultation procedure.
- Develop a method to assess administrative burdens on business.
- Continue the work on developing indicators of regulatory quality.

- Continue to exchange of best practices on better regulation between national authorities, in particular on impact assessments, inter alia within the Directors of Better Regulation Network.
- Take the necessary action to ensure that the European Business Test Panel is effective as one of the means of consulting business on EU policy and legislation.

#### 4.1.2 The Life Sciences and Biotechnology Strategy for Europe

In 2002 the Commission recognised in its communication on a strategy for life sciences and biotechnology that Europe does not have a single policy for life sciences and biotechnology but a patchwork of specific regulations, overlaid by many sectoral and horizontal policies at international, Community, Member State and local levels. The Commission therefore proposed to monitor progress in policy development and to anticipate emerging issues, to review the coherence across Community legislation and policies directly regulating, or indirectly impacting the development and application of life sciences and biotechnology. Particular attention would be given to ensure that regulation on life sciences and biotechnology adequately integrates international objectives and facilitates innovation and competitiveness. The general foresight function across Commission services would be enhanced for early identification of newly emerging issues, as well as its monitoring and review function to assess:

- The relevance, coherence and effectiveness of legislation and policy.
- The extent to which policy objectives are achieved and legislation enforced.
- The societal and economic impacts of legislation and policy measures.

Member States were called upon to also provide enhanced foresight/review functions and a co-ordinated interface for a dialogue on these issues. The Commission further indicated that the results of monitoring policy development and reviewing coherence would be presented in regular Life Sciences and Biotechnology Reports, including a rolling work programme for legislation.

Given the Commission's actions for the drafting and completion of various pieces of legislation for life science and biotechnology, the CBAG noted in 2003 that new or improved EU legislation must be as good or better than that of Europe's main competitors, in order to truly raise competitiveness. Requirements for industry to comply with legislation should be proportionate and should strike the right balance between the enabling and controlling objectives. In addition, legislation should particularly take due account of Small and Medium Enterprises (SMEs), which are a vital part of the biotechnology community. For them, according to the CBAG, requirements and procedures, which are manageable by larger companies, might represent a major obstacle or even a dissuasion to engage in certain activities.

In its second progress report of 2004 the Commission indicated more active co-operation from all Member States was needed in the new legislation governing GMOs. Having demanded, and subsequently committed themselves to a more rigorous framework, the Commission felt it was now imperative that all Member States implement the basic

Directive 2001/18/EC and the two Regulations on traceability/labelling and GM food and feed.

## **4.2 Coherence and impact of EU legislation for biotechnology**

The implementation of both EU regulatory frameworks for healthcare biotechnology products and for agro-food biotechnology products requires an efficient and effective functioning of the interfaces between product-specific legislation and GMO legislation. Notably, at these interfaces the Commission, the EMEA, the EFSA and Member States have difficulties finding a common position on the ERA requirements in the context of centralised assessment and authorisation procedures. Moreover, for field trials with GM crops, contained use of ‘self-cloned’ micro-organisms, environmental releases of GM vaccines or gene therapy product clinical trials, there are national differences in regulatory approaches. Obviously, these national differences need harmonisation throughout the EU, in order to improve regulatory certainty from an innovator’s point of view. Thereby it is urgent to arrive at a common implementation of the ERA requirements for authorisation of research and development of GMOs and their placing on the market as products.

Moreover, in the light of scientific progress, resulting in novel techniques to induce permanent change of organisms’ genomes, there will be a continuous need for the Commission and Member States to determine whether a certain novel technique for genetic alteration of organisms leads to a GMM/GMO in the meaning of the contained use and deliberate release Directives.

The deliberate release Directive foresees that the Commission should report on the experience acquired with its implementation in 2003 and thereafter every three years. As regards socio-economic implications the first report noted a steep decline in annual number of Part B fields trials with GM crops in the EU from 1997 to 2002. According to the Commission, this might be due to the fact that the new regulatory framework was under development, or due to fears of malicious damage of field trials in several Member States. It could also indicate a weakening of the European research base in this area. The report further noted that industry considered the stricter (ERA) requirements a substantial regulatory burden. This would also be seriously disadvantageous to SMEs and public research institutions to bring products to the market. In particular, the requirement to provide location details of field trials caused concern about the possible malicious destruction of these GM crops. Other socio-economic concerns were that the EU regulatory framework might have an adverse impact on producers in developing countries, the possibility of a brain-drain from Europe, of a decrease in scientific activity and of a reduction in interest by students to train in this publicly controversial research field, and finally the related possibility of a loss of competitiveness.

Furthermore, associations of biotechnology companies and food and feed industry expressed serious concerns about the GM food and feed Regulation and the traceability and labelling Regulation before their adoption in 2003. In their view, these Regulations

would not be workable, controllable and enforceable, in particular with a view to the labelling of (imported) food and feed ingredients derived from GM crops, which do not contain the detectable presence of ‘modified’ DNA and/or protein. Moreover, these Regulations would be disadvantageous to SMEs because of the high administrative burden involved.

In 2003 the CBAG indicated that European agro-food biotechnology, both in academia and industry, was lagging behind the US, Canada, Argentina, Brazil and other parts of the world in the use of modern-biotechnology derived crops, which would offer both socio-economic and environmental benefits. While this was considered partly due to a majority of the European population wary of the use of genetic modification in agriculture, another reason is the failure of the EU to have in place a sound science-based regulatory framework for GMOs. According to the CBAG, the EU regulatory framework is disabling rather than enabling, discriminatory rather than non-discriminatory, inconsistent rather than consistent in its application, and opaque rather than transparent in its implementation.

Since both Regulations only came into force in April 2004, the experience acquired with their implementation is limited so far. Nonetheless, within one year from now, that is no later than 7 November 2005, the Commission must also report on the implementation of the GM food and feed Regulation, accompanied, where appropriate, by any suitable proposal.

### **4.3 Main findings and issues to be further addressed**

- When monitoring and reviewing the implementation and enforcement of both EU regulatory frameworks for healthcare biotechnology and agro-food biotechnology, the Commission and Member States should aim at a simplification of both regulatory frameworks within reasonable time scales. For that purpose, a common and flexible methodology needs to be further developed and eventually adopted for an integrated socio-economic assessment of EU legislation for healthcare biotechnology and agro-food biotechnology before their adoption and during their implementation, with a particular emphasis on enhancing the competitiveness dimension. Given the global markets for healthcare biotechnology and agro-food biotechnology products, there is also a need to develop and adopt a common and flexible methodology for benchmarking the EU regulatory practices in comparison to regulatory practices in countries, like the USA, Canada, Argentina, Brazil, Japan, China etc. Findings from such benchmarking could contribute to further improve the EU regulatory practices for life sciences and biotechnology.
- The Commission and Member States should also develop and adopt a common and flexible methodology to assess administrative burdens on business and research institutions of EU legislation for life science and biotechnology. The Commission and Member States should also further continue the work on developing indicators of regulatory quality, as well as the exchange of best practices on better regulation for

life sciences and biotechnology between national authorities, in particular on impact assessments, inter alia within the Directors of Better Regulation Network.

- The information relevant to an integrated socio-economic impact assessment, to an assessment of the administrative burden, to a comparison of best practices and to an international benchmarking should thereby be made available to the public in the context of consultation in order to maximise the benefits of the consultation procedure. Actions should be taken to ensure that the European Business Test Panel and the CBAG remain effective as one of the means of consulting business on EU policy and legislation in the field of life sciences and biotechnology.
- For the review of the implementation of the GM food and feed Regulation and the traceability and labelling Regulation, on which the Commission must report not later than 7 November 2005, an integrated socio-economic impact assessment, an assessment of the administrative burden to business, an assessment of the regulatory quality and an international benchmarking could provide solid insights into the workability, controllability and enforceability of this Regulation.
- In order to create a legally predictable operating environment for business and research institutions, there is a need for adoption by the Commission, the EMEA, the EFSA and Member States of a common implementation of the ERA requirements for authorisation of research and development of GMO-derived products, as well as their placing on the market under both product-specific legislation and GMO legislation.
- In the light of scientific progress, resulting in novel techniques to induce permanent change of (micro-)organisms' genomes, there will be a continuous need for the Commission and Member States to determine whether a certain novel technique for genetic alteration of an (micro-)organism leads to a GMM/GMO in the meaning of the contained use and deliberate release Directives.