

**Directive 90/219/EEC: period September 1992 - August 1995**  
**BELGIUM : Report on the aquired biosafety experience (Art. 18.2)**

Belgium has nearly implemented the directive on the contained use of genetically modified micro-organisms (GMM) in the three regional legislations and already applies it in the Flemish and the Brussels-Capital Regions. The data provided in this report originates from official handling of dossiers and from the much more numerous contacts between the competent authorities and the notifiers including those of the Wallonian Region.

In order to harmonize the practical application of the directive, a co-operation agreement has been negotiated between 1990 and 1994 between the Regions and the Federal State and was signed on May 19, 1995. The wording of the agreement has been further improved according to the requirements of the Council of the State in August 1995. The amended agreement is now in the process of being legally approved by the federal and regional parliaments.

**The co-operation agreement, the Biosafety Advisory Council and the SBB.**

Briefly, the agreement establishes the general principles of a co-operation for an harmonised legal, administrative and scientific application of directives 90/219/EEC and 90/220/EEC in coordination with the more product-specific directives related to agricultural, food, feed, additives, medicinal products and by-products as examples.

The agreement defines a common system of scientific assessment of the biosafety of genetically modified and/or pathogenic organisms and the uses thereof. It is articulated around two structures:

- the Biosafety Advisory Council (the Council) which is the formal committee of the representatives of the competent and concerned authorities assisted by ad hoc working groups of commonly recognised experts. Presently, four working groups of experts are being implemented ( Recombinant viral vectors, virosomes, Vaccination & Gene therapy / Transgenic plants / Novel Food/Feed / Biotechnological safety norms).

- the Service of Biosafety and Biotechnology (SBB) located at the Institute of Hygiene and Epidemiology which carries on several risk assessment expertise tasks, the secretariat of the Council and laboratory research on specific biosafety generic questions . The SBB is a focal contact point for the OECD and the European Commission and a technical co-ordination interface between the belgian users and the competent authorities. It is also a documentation and archives center for biosafety. Parts of these documentation and archives was very recently provided on the internet through a Web server named "Belgian Biosafety Server" at <<http://biosafety.ihe.be>>.

Practically, the SBB is a normative public service carried out by a multidisciplinary core of height scientists of post-doctoral level co-financed by the Regions and the Federal State.

## **The Regional implementation of the european regulation on the contained use of GMM.**

Directive 90/219/EEC aims to protect human, animal and plant health and the environment when genetically modified micro-organisms are used for any purpose in contained installations.

The three regions and the federal state have agreed on common scientific criteria for risk assessment and containment facilities harmonized with requirements of other directives related to worker protection, animal welfare, animal sanitary police and phytosanitary police. This is a first major achievement of the Belgian biosafety acquired experience, based on the inter-networking of most of the legal and scientific aspects of biological safety managed more or less specifically by different regional or federal authorities.

The Flemish and the Brussels-Capital Regions have implemented the Directive and published their legislation in the Official Journal (25/01/94 for the Region of Brussels-Capital and 31/07/95 for the Flemish Region). A similar legislation is close of being approved by the Wallonian government. In the meantime, the information phase of major installations and the preparation of the administrative application of the Wallonian regulation is already being carried out.

Each Region has integrated the biosafety provisions into the frame of their general legal frame regulating classified installations leading to environmental permits or exploitation permits. As such, biological safety becomes just an additional safety issue among the others to which a classified installation or activity must conform and an useful parameter of the developing total quality insurance practices.

### **General principles of the regional regulations.**

1. In accordance with the spirit of the european regulation, the safety of MGM-based operations carried out in contained installations is assessed through a general information system carried out by competent administrations.

2. As defined by the directive, the regional regulations applies to “installations” (article 8) and to the “operations” carried out in such installations (Article 9). An operation is defined on a case by case according to the user context: in an academic context, an operation applies to research or development generic projects or programs. It is thus wide in the sense that it can not only integrate various gene donors, acceptors, genes, vectors, ... for a given operation but also unpredicted biological tools at time of notification. Any operation, in the frame of article 8 or 9 of the directive, can be carried for 5-10 years irrespective to the containment levels concerned provided the goals and the safety level of the containment facilities and biological tools and products remains stable. In an industrial context, an operation scope is usually narrower and even restricted to the exploitation of a very well defined GMM or a family of GMMs differentiated by known or parameters unpredictable within known safety-unrelated limits.

As second experience achievement, the Belgian regulatory practices are basically preventive at start of activities, the regulatory pressure being decreased or suppressed afterwards over very long periods of time, an option better fitting with the very rapid-evolving tools and competitiveness requirements of the R&D operations.

3. The regional regulations have integrated the provisions of directive 90/219/EEC in the scientifically larger frame of “biosafety”, in which all living organisms bearing risks for human health, the environment and the biodiversity are concerned. Consequently, the regulations include criteria and procedures not only for the contained use of GMM but also for genetically modified organisms (GMO and the uses of human, animal and plant pathogens. The regulations provide reference lists of more than 2000 pathogenic, opportunistic or allergenic micro-organisms, their maximal theoretical class of biological risk and -when defined by scientific experience- the required containment level. These list are used to help the notifier to assess the safety practices of his operations on ground of established records of microbiological safety should these organisms be concerned by his operations as such, as gene donors or gene acceptors.

4. Like a majority of states, The system of four classes of biological risks and the related four containment level is applied, as it is already the case in the United States since 1976, at the WHO,

in Japan and in most of the European member states for quite a long time. Group I MGM are handled in containments of level 1 whereas group II GMM are handled at containment levels 2, 3 or 4. It is observed that sub-dividing containment levels into levels 2-4 allow a more realistic, easier and cheaper management of group II GMM-based operations.

5. Two means are guaranteeing the best fit between legal requirements and the real estimated risks of an operation were introduced in the regional regulations:

- when used as reference, the classes of risks of the pathogens are maximum theoretical levels.

Such level of risks are known not to be reproducible in all ecosystems, in all types of operations and are very often the result of a very opportunistic combinations of heterogeneous climatic, geographical and biological factors influencing both the pathogen and his naturel targets on one side and the sanitary status of the target at time of biological interaction with the potentially pathogenic organism. Therefore declassification criteria have been established for the containment of GMM derived from animal and plant pathogens and elements thereof. Inversely, transduction of transgenes in multicellular gene acceptors may rise physiological and genetical questions theoretically potentializing the risk of an operation. Applying the precautionary principle may lead to an increase, even transient, of the containment level, for example when no safety records after animal testing are available.

- By “containment” it is understood a operation-specific combination of physico-chemical barriers, safety facilities, good practices and worker training conditions on the geographical site of the host installation. These containment parameters are described for laboratories, animal husbandries, greenhouses, hospital rooms for human gene therapy and vaccination and for large-scale production units.

As an illustration, such provision might allow the routine diagnostic of non-airborn pathogenic GMM of class of risk 3 to occur in laboratory containments of level 2 with laboratory practices of level 3.

6. GMMs can be certified as class of risk 1 organisms or fulfilling the OECD G.I.L.S.P. (Good Industrial Large Scale Practice) status according to the criteria of Annex II (new and old versions respectively). On the same way, GMMs or GMOs can officialy be exempted (at user’s request) of the application of the regulations according to the criteria of Annex I B or Annex II.

7. The decision of the competent authority following the notification of an operation must be given within the same delays as those defined by Directive 90/219/EEC. However, the scientific evaluation of the biosafety dossier, which is reported by the SBB eventually after advice of the Biosafety Advisory Council, must be adressed to the competent authority at last 45 working days after submission of the notification for a first use dossier (article 8), and after 30-45 days (according to the type of operation) after submission of common notifications (article 9).

8. The notification dossier is based on forms and guidelines and dealt into a “technical dossier” and a “public dossier”. A technical dossier is required both for the first use permit and notification procedures whereas the public dossier is only required along the first use procedure.

The “technical dossier” is the scientific evaluation tool for the SBB and can contain confidential data. The unique exemplar of this dossier is submitted to administrative classification whose access is restricted to a limited number of defined persons designated by the competent authorities. The “public dossier” is similar to the technical one but written in common language. It is by definition transparent and may be submitted to public hearing according to current legal rules.

### **Belgium acquired-experience.**

Due to the delayed implementation of Directive 90/219/EEC in Belgium, the number of dossiers handled by the competent authorities is estimated as one tenth of the theoretical total at time of reporting.

From January 1994 to August 1995, 24 dossiers were reviewed by the SBB within the scope of the existing regional regulations, with the following distribution:

- 3 dossiers of request for exemption of GMMs under the criteria of Annex I B ;
- 2 dossiers of request for certification of GMMs in class of risk 1 under the criteria of Annex II;
- 19 dossiers of contained use of pathogens, GMMs or GMOs, involving a total of 86 operations.

Among the 86 operations, 28 dealt with GMMs, the others concerning GMO's or pathogens only. The two charts provided as annexes I and II illustrate respectively the distribution of these operations as a function of the type (A or B) of operation and the class of risk of the GMM, and the distribution of the operations according to the final containment level required.

The average time required by the SBB to report its scientific advice to the competent authorities is about 33 working days per dossier (a dossier can include several operations). This average does not take into account the period of time during which the competent authority is awaiting for complementary information. Although standardized template forms for the dossiers (both on paper and electronic support) are provided to the notifiers, and despite the basic information provided to notifiers or local Biosafety committees along audits or seminars, the SBB is permanently submitted to information requests as a result of the very specific nature of the operations and combination thereof inside a given installation. This essentially reflects the difficulty for scientists, mainly from academic area, to cope with the legal wording of the regulations and with biosafety strategies applied to local complex situations. At the level of big installations there is usually a lack of coordination between the local administration and the scientific users which impairs the smooth preparation and deposit of the dossier.

The competent authorities are currently working on the improvement of this time-consuming situation through several measures:

- a better preliminary information of responsible user's administrations, notably through concertation with local biosafety committees ;
- a more interactive style of the template forms on the base of the acquired experience;
- the publication of guidelines related to these forms and to specific aspects of biosafety (like the risk assessment);
- the delivery of such informations on the Internet, providing transparent on-line scientific and administration information to the notifiers.

These measures should speed-up the information and authorization procedures, improve public acceptance and reduce to a minimum the administrative contribution of the notifiers.