

**SUMMARY REPORT ON THE EXPERIENCE OF BELGIUM
WITH DIRECTIVE 90/219/EEC AS AMENDED BY
DIRECTIVE 98/81/EC**



(TRISANNUAL REPORT UNDER ARTICLE 18 OF DIRECTIVE 90/219/EEC,
AS AMENDED BY DIRECTIVE 98/81/EC)

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Annex : Contained uses of GMMs of risk class 3

1. Transposition of Directive 98/81/EC into national legislation

The regulatory framework concerning the contained use of genetically modified micro-organisms (GMMs) is implemented and enforced in Belgium at the regional level. It means that three instruments of transposition (one decree per Region) have to be published.

The regional regulatory frameworks implementing Directive 90/219/EEC already covered most of the provisions contained in Directive 98/81/EC. The main objective of the transposition was thus to revise these regional decrees to fully implement the new provisions of the Directive, and also to better take into account certain aspects such as the acquired experience, the increasing needs regarding public information and participation and the precautionary principle.

Although the integration of the provisions of Directive 90/219/EEC within the general framework of the regional environmental laws for classified installations had caused difficulties in the administrative implementation of the legislation, it was decided to keep this initial choice for the transposition of Directive 98/81/EC.

According to the "Cooperation Agreement" on the administrative and scientific coordination concerning biosafety" of 25/04/1997, the transposition and implementation of the "contained use" Directives shall be done in a harmonised way between the three Regions (further details on this cooperation agreement have been given in the previous trisannual report and are also available from the "Belgian Biosafety Server" - <http://www.biosafety.be>). Consequently, the first step in the transposition has been to define (through discussions at the administrative and technical levels) the points of harmonisation on the basis of which the Regions should move forward in the transposition of Directive 98/81/EC.

On this basis, the Brussels Region was then the first to finalise its regional decree transposing Directive 98/81/CE (*Belgian Official Journal of 26.02.2002, p. 7209*). The decree provides for detailed procedural and technical requirements for contained use activities involving GMOs (including GMMs) and/or pathogens.

In the Walloon Region, the above-mentioned points of harmonisation were only partly taken into consideration. A regional decree transposing Directive 98/81/CE was published in September 2002 (*Belgian Official Journal of 21.09.2002, p. 41711*). This publication coincided with the achievement of a large revision of the general environmental regulatory framework and the full application of the new environmental permit. The legislation related to contained use of GMOs and pathogens was thus drafted as a sectoral decree embedded into the legislation covering the environmental permit. As a result, the decree transposing Directive 98/81/CE gathers normative information only whereas administrative and procedural requirements are described in the framework of the environmental permit.

The implementation is not fully completed yet in the Flemish Region, mainly for juridical reasons. A proposal of decree was approved by the Flemish parliament in June 2002 but was withheld by the Council of State because the actual environmental permit didn't give a proper juridical base for the implementation of directive 98/81/EC. Following this a modification of the decree concerning the environmental permit has been submitted to the Flemish Minister of Environment to integrate the remarks of the Council of State. However, as mentioned before, the Flemish decree implementing Directive 90/219/EEC already covers most of the provisions contained in Directive 98/81/EC.

2. Notification and approval systems

2.1. Regulatory and advisory systems

The regulatory and advisory systems remained unchanged since the last trisannual report (September 1999). Please refer to this report and to the "Belgian Biosafety Server" (<http://www.biosafety.be>) for further details.

2.2. General procedures for notifications and authorisations

In the three Regions, the contained use of GMMs, GMOs and/or pathogens is a classified activity requiring an Environmental Permit.

The notification and approval systems established in the regional decrees based on the transposition of Directive 90/219/EEC (and subsidiary Directives and Decisions) remained applicable until 25 February 2002 in the Brussels Region and until 20 September 2002 in the Walloon Region and still applied at the end of 2002 in the Flemish Region (see chapter transposition of Directive 98/81/EC into national legislation).

Please refer to the previous trisannual report (September 1999) for further details about these systems.

When the notification procedures in the above-mentioned decrees were more or less similar between the three Regions, the situation changed with the adoption in the Brussels and Walloon Regions of new regional decrees transposing Directive 98/81/EC. The main procedural requirements of these new decrees are described hereunder. It must be noted however that, due to the late entry into force of these legislation, very limited experience has been gained with their practical implementation.

In the Brussels Region, the new Decree foresees, as Directive 98/81/EC does, two types of procedures, respectively for first contained uses and for subsequent contained uses. The advice of the technical expert (namely the Service of Biosafety and Biotechnology) is a compulsory step in both types of procedures.

In order to get an authorisation for a *first contained use*, the notifier shall submit a "biosafety dossier" before starting such use. The content of the biosafety dossier is in line with the requirements of Annex V of Directive 98/81/EC and shall contain a risk assessment of the contained use according to Annex III of the Directive. The biosafety dossier is based on official forms and guidelines developed by the SBB and the competent authority, and is composed of a "technical dossier" and a "public dossier".

The "technical dossier" is the scientific reviewing tool for the SBB and can contain confidential information. The "technical dossier" exists as a unique exemplar, submitted directly to the SBB by the notifier, and accessible to a limited number of persons designated by the competent authority.

The "public dossier" is a summary of the technical dossier written in common language and submitted to the SBB and the competent authority. It is by definition transparent and is made available by the regional authority for public hearing.

A first class 1 contained use may proceed the day following the notification to the competent authority.

A first class 2 contained use may, in the absence of any indication to the contrary from the competent authority, proceed 45 days after the notification, or earlier with the agreement of the competent authority.

A prior written consent of the competent authority is needed to carry out a first class 3 or 4 contained use.

Subsequent contained uses shall also be notified in advance. For subsequent class 1 contained uses, only a "technical dossier" has to be submitted to the SBB. For class 2 or a higher class of contained uses, a full "biosafety dossier" is needed along the same procedure as for first contained uses.

A subsequent class 1 contained use may proceed the day following the notification to the SBB.

A subsequent class 2 contained use may proceed the day following the notification, provided that the premises have been the subject of a previous notification to carry out class 2 or a higher class of contained uses and that any associated consent requirements have been satisfied. The applicant can, however, himself request a decision on a formal authorisation from the competent authority. In this case, the decision must be made within a maximum of 45 days from the notification.

A class 3 or higher class of contained use may not proceed without the prior written consent of the competent authority, which shall communicate its decision:

- at the latest 45 days after the notification, in the case the consent requirements associated with the subsequent contained use have been already imposed and satisfied for a previous contained use, and that this previous contained use has taken place in the same premises;
- at the latest 90 days after the notification, in other cases.

From the previous paragraphs, it can be concluded that the procedural requirements in the Brussels Region exactly follow those foreseen in Directive 98/81/EC, with the exception of subsequent class 1 contained uses which require further notification according to the regional decree.

In the Walloon Region, the new Decree is a sectoral legislation of the new main legislation related to the environmental permit. One of the consequences of this political choice is that the procedural provisions of Directive 98/81/EC (articles 7 to 10) have not been implemented as such in the Walloon Region. Indeed, all administrative and procedural requirements for contained use activities are described in the main legislation related to the environmental permit. There is no distinction between first and subsequent contained uses, and the deadlines for authorisations are those applying for the delivery of the environmental permits.

In order to get an environmental permit for premises where (a) contained use activity(ies) take(s) place, the notifier must submit a dossier containing an assessment of the contained use(s) as regards the risks to human health and the environment that the(se) contained use(s) may incur, using as a minimum the elements of assessments described in Annex III of Directive 98/81/EC. The dossier must also contain the advice of the technical expert (namely the Service of Biosafety and Biotechnology) concerning this evaluation.

2.3. Certification

Contained uses of GMMs or GMOs generated by means of the techniques or methods described in Annex II, Part A of Directive 98/81/EC are excluded from the scope of the regional decrees, provided that these GMMs or GMOs have been certified by the technical expert (namely the Service of Biosafety and Biotechnology) as complying with the provisions of this Annex.

3. An overview of activities and installations (GMOs as well as GMMs)

3.1. Reviewed installations and operations

During the period 1999-2002, 223 dossiers of installations have been reviewed by the SBB acting as the advisory body. At time of report six dossiers, received in 2002, are still under review by the SBB and involve 24 contained uses.

These dossiers have the following distribution:

- 1 dossier of request for exemption of GMMs under the criteria of Annex II, Part A of the Directive 98/81/EC
- 222 biosafety dossiers of installations, covering 551 contained uses of pathogens, GMMs and/or GMOs (transgenic plants and animals). 18 operations fell out of the scope of the regional decrees on contained use: these concerned either the use of non genetically modified cell cultures or the production of monoclonal antibodies.
- Among the 551 reviewed contained uses, 158 operations exclusively concerned non genetically-modified, pathogenic micro-organisms.
- With respect to contained uses of GMMs and GMOs, 153 dossiers covering 393 operations have been assessed.

These GMM/GMO dossiers are distributed as a function of:**- The procedure and the administrative year****Table 1:** Distribution of the number of installations (number of contained uses) as a function of the procedure and the administrative year.

Procedure	Year	1999	2000	2001	2002*	Total
First contained uses		16 (63)	24 (87)	12 (50)	11 (30)	63 (230)
Subsequent contained uses:						
New operations		8 (12)	14 (20)	17 (33)	21 (32)	60 (97)
Modifications of operations		7 (8)	6 (14)	4 (7)	3 (3)	20 (32)
Renewal of operations		0	0	1 (4)	2 (7)	3 (11)
Subtotal					37 (72)	146 (370)
Notifications in Wallonia in 2002*						7 (23)
Total		31 (83)	44 (121)	34 (94)	44 (95)	153 (393)

*** remark: since the new Walloon decree of 18/4/2002 concerning the contained use of GMOs and/or pathogens doesn't distinguish anymore between first and subsequent contained uses, only the total number of activities is given for this region for the year 2002.**

Table 1 illustrates the evolution of the application of the regulations. In comparison to the years following the implementation of the first contained use Directive 90/219/EC, the number of notifications introduced under the "subsequent contained use" procedure is now overtaking the notifications introduced under the "first contained use" procedure.

- The Competent Region:

Brussels: 27 dossiers, 63 operations

Flemish Region: 100 dossiers, 225 operations

Walloon Region: 26 dossiers, 105 operations

The number of dossiers submitted in the Flemish Region significantly increased in 1999 and remained high during the following years. In the two other Regions however, the process was reversed: the highest numbers were reached in respectively during the period 1994-1999 and decreased during the period 1999-2002.

The 393 operations of contained use of GMMs and/or GMOs are distributed as follows:

- GMMs and/or GMOs
- GMMs: 230 operations
- GMOs: 42 operations
- GMMs and GMOs: 121 operations

One single operation can involve the use of both GMMs and GMOs)

- Types of GMOs:

Transgenic animals: 63 operations
Transgenic plants: 99 operations

- Biological risk class, (art 5, 3 of Directive 98/81/EC)

One single operation can imply the use of GMMs and/or GMOs of different biological risk class. This explains why the total of contained uses is higher than 393 :

Risk class	GMM	GMO
1	325	157
2	200	0
3	9	0
4	0	0

The number of operations using GMMs of class of biological risk 1 and 2 is predominant. Only 9 operations implied the use of GMMs of risk class 3 (genetically modified HIV, chimaeric viruses, adenoviruses, retroviruses, *E. coli* containing Hepatitis C virus constructs, and genetically modified *Trypanosoma*). There are no contained uses of biological risk class 4. A detailed description of contained uses of risk class 3 is given in annex.

3.2. Extend of application of the biosafety regulation

Although the number of installations and activities reported in 3 and in the previous report do not cover all existing ones, a maximum of contained uses have been notified during the last years.

The biosafety regulation of premises and associated activities is now well settled in Belgium. The advisory body acquired a significant scientific and regulatory experience in the risk assessment of GMM/GMO-related operations and installations. The administrations have gained a training of the technical complexity of biosafety through their contacts with the notifiers and the SBB.

4. Risk assessment and classification of contained uses

An assessment strategy has to be followed by both the notifier and the advisory body that is defined in the regulations. The assessment is an “installation by installation - operation by operation” process.

4.1 Assessment of the class of risk of an operation in a given installation

As defined by the Directive, the regional regulation applies to “installations” and to “contained uses” or “activities” carried out in such installations.

The biological risks of each operation involving the contained use of GMOs and of their related potentially pathogenic gene receptors or gene donors are assessed taking several risk assessment data into account (see 4.2).

The risk assessment ends with the classification of the operation into one of the 4 classes of risk provided in Art. 5 of Directive 98/81/EC.

4.2. Risk assessment data

Belgian regulations implementing Directive 98/81/EC have integrated as such the annex III of the Directive devoted to principles to be followed for the assessment referred to in article 5 (2). They also refer to the guidance notes for risk assessment outlined in Annex III of Directive (Decision 2000/608/EC of 27 September 2000).

The following technical annexes have been added to the aforementioned annex (Annex III, 1st part in the Belgian regulations) to give some more precision to perform the risk assessment:

Annex III, 2nd part: Criteria for classifying GMMs (Commission decision 96/134/EC of 16 January 1996) and GMOs (animals and plants) into risk class 1.

Annex III, 3rd part: viral vectors, inserts and cell cultures, their class of biological risk, the corresponding containment levels and definition of the biological, epidemiological or genetic factors potentialising or reducing the level of biological risk under proposed operation.

Annex III, 4th part: reference lists and biological class of risk of human, animal and plant pathogens. These lists provide the risk class of about 2,500 pathogenic, but also opportunistic or allergenic (micro-)organisms.

4.3. Definition of an appropriate containment

The risk management addresses the definition of the best containment measures fitting with the risk assessment and the defined biological risk class of the operation in the context of the installation (building) and the specific staff involved. This includes data provided by the notifier about:

- the available physical primary (equipment), secondary (laboratory facilities) and tertiary (building design) barriers, together with the physical waste inactivation processes
- the chemical barriers used for disinfection or inactivation
- the biological barriers
- work practices including personal protective equipment, work organisation, rooms management, equipment management
- the applied norms for quality assurance (ISO 900x, ISO 45001/17025, GLP, GMP)
- the experience and training of the staff and the personal turn-over

In addition, in order to promote auto-inspection inside the installation, the Belgian regulations have made compulsory the nomination of a local biosafety officer as well as the forming of a local biosafety committee. Their respective tasks are listed in the regulation.

The risk management also includes the control of the compatibility between operations occurring within the same building: operations requiring a high degree of aerosol prevention must be physically located in the most access-restricted areas and the laboratory practices and personal training enhanced.

All these elements are contributing to assign the biosafety containment levels that reduces to an absolute minimum either the worker's exposure to biological agents and their risk of laboratory-acquired infection or any potential escape of GMMs or GMOs into the environment.

Along the reviewing process applied by the authorities, the precautionary principle is taken into account following the conclusions of the presidency of the European Council of 7-9 December, 2000 in Nice.

The combinations of containment criteria are listed in the annex IV of the Belgian regional regulations. This annex presents tables with the containment requirements for laboratories, animal units, glasshouses and growth-rooms, hospital rooms as well as for installations used for large scale process. A set of definitions is also included.

5. Inspections and enforcement issues

Inspectorates

Whereas the first years after implementation of the contained use directive the competent authorities focused on the authorisation process, biosafety policy gives now also an important place to inspection and control of contained uses of GMOs (and also pathogens). Several contacts with the regional competent authorities lead to decisions on collaboration between the SBB and the Inspection services with respect to training courses and general planning for inspections of installations. In 2002 and 2003, training courses were given to inspectors from the 3 regions.

The three regions show a different approach for their inspection planning. Whereas the Flemish Region foresees to inspect all authorised installations in the first place, the Walloon Region aims to inspect all installations concerned by the contained use regulation, also those who didn't notify their activities yet. On the other hand the Brussels Capital Region is starting to inspect first of all the installations with the highest containment levels in Belgium, which means containment level 3 premises.

6. Problems with interpretation of the provisions (possibly with conflict in defining work use with respect to Directive 90/220/EEC/Directive 2001/18/EC)

Certain terms or provisions in the Directive have generated problems of interpretation and/or of practical application:

It is not always clear what must be considered or not as a "subsequent contained use". There is no definition of a subsequent contained use in the Directive. The regional regulation for Brussels Region implementing Directive 98/81/EC has defined the concept of subsequent contained use as "any new contained use, modification of contained use or continuation of contained use in an installation which has been the subject of a previous notification or authorisation for a contained use of the same or a higher class of risk". Nevertheless the notifier does not always know from which moment modification of their activities form a subsequent contained use.

7. Clinical trials using the provisions of the Directive

Clinical trials activities can be authorised within the Regional biosafety regulations as soon as they involve GMMs and if the treatment occurs in a contained area (hospitals).

Since 1999, eight human clinical trial protocols have been approved in Belgium within the Regional biosafety regulations and one application is presently under review. In new cases, the risk assessment has always involved meetings of an ad hoc scientific Committee of the Biosafety Advisory Council.

Six of these trials were multicenter and two of them unicenter. All were carried out in academic hospitals.

Seven of these protocols intended to test viral vectors, and one of them a genetically engineered bacteria.

Seven of them aimed cancer therapy and one of them to treat infectious disease.

More information on the regulatory parameters of these protocols and the most relevant clinical data of the authorised trials can be found on the "Belgian Biosafety Server" (<http://biosafety.ihe.be/GT/regulatory/GTtrials.html>).

8. Public consultation and information

The Regions decided that the procedures for public consultation in force within the framework of the regional environmental laws for classified installations adequately covered the implementation of Article 13 of the Directive. Consequently, no specific measures have been established in the legislations concerning the contained use of GMOs and/or pathogens.

The procedures for public consultation aim at providing general information to the neighbourhood regarding the contained uses. In the Flemish and Brussels Regions, this information is given via a "public dossier", which is a short summary of the full notification drafted by the notifier and containing information written in standard language and without any reference to confidential information.

The consultation also gives the public the possibility to express comments, observations or objections regarding the contained uses. The competent authorities take these comments, observations or objections into account when drafting their final decision. All decisions are made available to the public for a time-limited period. Appeals against decisions may be submitted to the competent authority within that period.

Public information is ensured primarily via the "Belgian Biosafety Server" (<http://www.biosafety.be>), the Internet site maintained by the SBB. This Web site provides to the notifiers and the general public scientific and administrative information such as full text of regional laws and EU Directives, procedural aspects, co-ordinates of competent authorities, notification forms, guidelines and a huge list of laboratory biosafety resources. To improve the implementation of the new decrees transposing the Directive 98/81/EC, more specific public information/consultation tools could be developed on the Web site in the future.

9. Accident and emergency plans

Emergency plans

Following Article 14 of the Directive, an emergency plan must be drawn up for contained uses where failure of the containment measures could lead to serious danger, whether immediate or delayed, to humans outside the premises and/or to the environment.

Thus, it is not clearly mentioned in the Directive for which classes of contained uses an emergency plan is compulsory, and the type of information that must be given on such emergency plans is not clearly defined.

In Belgium, the Flemish regional regulation (Flemish Decree of 1/6/95) implementing Directive 90/219/EEC mentions that the user must submit the information needed to establish emergency plans outside the contained installation in cases of type B operations with a class of risk 2, 3 or 4.

The Brussels regional regulation (Brussels Decree of 8/11/2001) implementing Directive 98/81/EC mentions that the user must submit the information needed to establish emergency plans outside the contained installation in case of operations with a class of risk 2,3 or 4. Before the beginning of a contained use the regional authority consults the competent federal authority (Federal Public Service Interior) in order to set up emergency plans outside the contained installation.

The Walloon regional regulation (Walloon Decree of 4/7/2002) implementing Directive 98/81/EC mentions that the user must submit an emergency plan (project) outside the contained installation for contained uses of class of risk 2, 3 or 4.

Accidents

The three regional regulations mention that the user must declare immediately to the competent authority an accident that occurs in a contained use installation (the information to be provided in such a case is listed in annex of these regulations).

Until now, no accident has been declared in Belgium.

10. Protection of confidential information

In accordance with article 19 of Directive 98/81/EC, the new regional decrees transposing the Directive in the Brussels and Walloon Regions give the possibility to the notifier to indicate, when necessary, the information in the notifications submitted pursuant to the decrees that should be treated as confidential.

However, the following information can in no case be regarded as confidential:

- the name and address of the notifier;
- the description of the GMMs, GMOs (or pathogens)
- the class, the objective and the site of the contained use, and the measures of containment;
- the evaluation of foreseeable effects, in particular any pathogenic or ecologically disturbing effects;
- any information already published in the press or by a patent office.

Although Directive 98/81/EC has still to be fully implemented in the Flemish Region, the current legislation on the contained use of GMOs and/or pathogens already provides requirements on confidential information that are consistent with the provisions of the Directive.

Confidential information must be gathered in a specific, distinct and identifiable annex of the notification dossier submitted to the SBB. Confidential information is never referred to in public advices or in authorisations.

Confidential information is maintained and archived by the SBB in secure premises.

The competent authorities and the SBB shall not divulge to third parties any information decided to be confidential and notified or otherwise provided, and shall protect intellectual property rights relating to the data received.

11. Waste disposal

In Belgian Regional regulation implementing Directive 98/81/EC, there is an explicit legal requirement to inactivate all types of GMOs - even of risk class 1- to be disposed of in wastes by appropriate and validated means.

In each region, these requirements are completed by specific regulations on waste originating from medical care and dangerous waste in general, imposing rules for storage, for incineration and for collection by an approved company.

Upon request of both the Federal Ministry of Agriculture and a company specialised in large scale production of GMMs, the SBB has evaluated the monitoring program for detection of living GMMs in sludge from their waste water treatment plant.

Since the contained use regulation in Belgium requires validated inactivation of all GMMs, including GMMs of risk class 1, the company needed an authorisation to use the waste originating from fermentation of GMMs as compost in agriculture.

However, the inactivation procedures can never exclude the potential presence of still a certain amount of living GGM. So the question was raised how to determine a threshold value for the amount of living GMMs allowed in waste arising from large scale production of GMMs. The SBB proposed as maximum acceptable emission levels for the discharge of GMMs in wastes $< 10^4$ organisms/g.

Annex

Contained uses of GMMs of risk class 3 (According to art. 18.1 of Directive 98/81/EC)

Nine class 3 contained use activities involving GMMs have been notified in Belgium in the period 1999-2002. These are the following:

Contained use 1

Description : this contained use activity implies the use of a chimaeric virus which is a combination of the C vaccine strain of the classical Swine Fever Virus (CSFV) and Hepatitis B virus, type 1B.

Purpose : in vitro screening of chemical drugs with respect to their activity against the chimaeric virus.

Risk : the risk associated with this contained use activity is potential production of infectious virus.

Contained uses 2 and 3

Description : these 2 different contained use activities imply the use of genetically modified HIV virus (mutations in genes coding for reverse transcriptases, proteases, integrases,...)

Purpose : study of resistance mechanisms against viral drugs

Risk : the risk associated with these 2 contained use activities is potential production of infectious virus.

Contained use 4

Description : this contained use activity implies the use of recombinant adenovirus derived from serotypes 5 and 16 and carrying as inserts human genes from cDNA libraries.

Purpose : study of function of genes playing a role in genetic disorders

Risk : the risk associated with this contained use activity is potential production of recombinant virus expressing genes coding for expression products playing a role in important physiological processes, mechanisms of cellular immortalisation, apoptosis, and genes coding for unknown expression products.

Contained use 5

Description : this contained use activity implies the use of a chimaeric virus, which is a combination of Simian immunodeficiency virus (SIV) and Human immunodeficiency virus (HIV).

Purpose : research project on the development of a vaccine against AIDS

Risk : the risk associated with this contained use activity is potential production of infectious and even pathogenic virus for man

Contained use 6

Description: this activity implies the use of genetically modified *Trypanosoma brucei rhodesiense* (genetically modified SRA gene) of the same risk class as the parent strain

Purpose : study of the antigenic variation of African trypanosoma's aiming at the development of a vaccine

Risk: the principal risk associated with this contained use activity is accidental inoculation of the infectious form of genetically modified *Trypanosoma brucei rhodesiense*

Contained use 7

Description: this activity implies the use of genetically modified *E. coli* non pathogenic strains (TOP 10, DH5alpha, XL1-Blue, HB101) and transfected mammalian cells (primary cultures from rat liver and human liver as well as the animal cell line HepG2) containing full length constructs of Hepatitis C virus.

Purpose: study of the functional genome of Hepatitis C virus in an in vitro cell culture model

Risk: the principal risk associated with this contained use activity is potential generation of infectious HCV virus in the transfected cell cultures.

Contained use 8 :

Description : this contained use activity implies the use of genetically modified retroviral vectors derived from MLV.

Purpose : study of the regulatory function of human viral transactivator on human CD3- γ gene transcription and the development of lymphoid malignancy.

Risk : the risk associated with this contained use activity is potential production of infectious retrovirus in the used cell cultures.

Contained use 9:

Description : this activity implies the use of retroviral vectors derived from MLV and lentiviral vectors derived from HIV-1. These vectors are carrying oncogens Tax and BcrAbl.

Purpose : study of the lentiviral-mediated dendritic cell transduction in the evaluation of immune mechanisms involved in chronic myeloid leukemia .

Risk : the risk associated with this contained use activity is potential generation of genetically modified infectious virus containing human oncogens.