3

1994 - USA

101 health care personals were infected by HIV

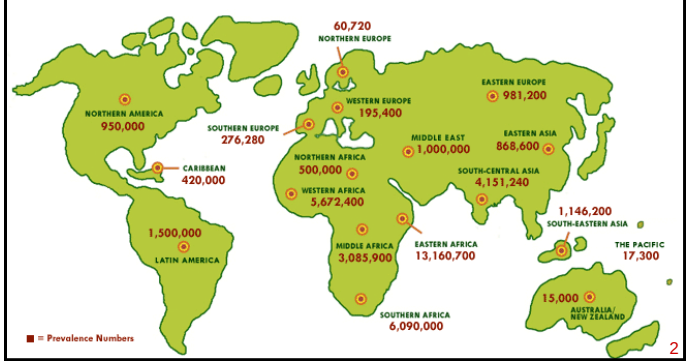
Nurse - 26
Laboratory technician - 25
Physician - 13
Medical technician - 7
Dentist - 6
Morgue technician - 3
etc.

2

Clinical Microbiology Reviews 8. 3. 389-405.

10 years later - 2004

42 million infections worldwide



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4

Biol(logical) Safety

1. lecture.: indirect (ecological)
2. ea.: direct (health)

} danger

•GMO's - Genetically Modified Organism's – problems of their applications

•Legal regulations

•Risk of biological infections (examples)

•Laboratory requirements

5

GMO =Genetically Modified Organism

Definnitions

Natural Organism
Any living organisms, which is able to reproduce and inherit its genes

Genetic Engineering:
Such a method, whic is able to remove a gene or genetic part from a donor cell, and transfer it into another host cell, resulting the changes of the later's natural genom

Genetically Modified Organism (GMO):
Such an organism, in which the genom was modified by genetic engineering, including its successor's (childran) having the same modified characteristic.

Law No.:1998. XXVII.

6

GMO

Activities considered as genetic modifications

Recombinant Nucleic Acid techniques, which includes the constructions of new recombinations of genes through *in vitro* (outside any living organism) incorporation of nucleic acid molecules into any of different vectors (like viral, bacterial, or plasmid DNA) followed by transfection into any hosts, not having the same attribution naturally.

Such techniques, which includes the direct implementation of such genes, which were constructed *in vitro* like: **microinjection, macroinjection and microencapsulátion;**

Cell fusion (incl. protoplast-fusion) or **hybridization techniques**, in which new recombination of genes are reached through the artificial fusion of two cells, and this resulted a new organism (which does not existed before)

Government regulation No. 148/2003. (IX. 22.)

7

GMO

Definitions

Experiment:
such a genetic intervention, in which the main goal is not to manufacture a product, but to reach the development of science in a closed system. Research aimed genetic engineering is considered as experiment, too.

Emission:
The dispension into the mother nature (i.e. environment) of any genetically modified organisms or their part or their recombinations.
The genemodifications done into a non-closed system is also considered as emission.

8

GMO

Definitions

Closed system applications:

„every activities, in which microorganism are modified with gene-techology, or in which genemodified microbes are cultivated, stored, transported, annihilated, disposed, or utilized via any other ways beside special containment directives to exclude the contact of GMO's with humans and the environment. "

Law No.: 2002. LXVII.

GMO

Closed System Applications

GMO

Closed System - subgroups

"A" type activities:
Inside closed system applications some small scale education, research or development aided, activities with non-commercial purposes are authorization/licence free!!!

"B" type activities:
Inside Closed system applications anything else then A-type activities are subject to authorization/licence.

82/2003. Decree of Ministry of Agriculture Appendix 4.: Requirements of License application for closed system application:

GMO

Authorities to inspect gentechological activities

Everybody on its area....

- National Institute for Agricultural Quality
- Plant and Soil Protection Central Service
- County Animal Health and Food Control Stations
- Consumer Protection Inspectorate
- National Public Health and Medical Officer Service, Chief Medical Officer
- Environment and Nature Protection Inspectorate

Governemnt decree No.:148/2003. (IX. 22.)

GMO

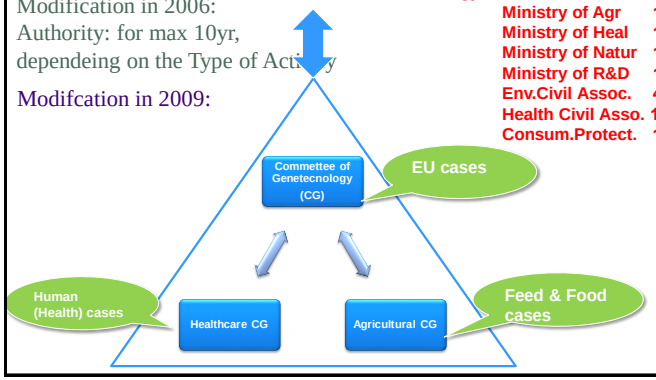
Authorities to inspect gentechological activities

Modification in 2006:
Authority: for max 10yr, dependeing on the Type of Activity

Modifcation in 2009:

Commettee of Genetechnology:

HAS	6fő
Ministry of Agr	1fő
Ministry of Heal	1fő
Ministry of Natur	1fő
Ministry of R&D	1fő
Env.Civil Assoc.	4fő
Health Civil Asso.	1fő
Consum.Protect.	1fő



13b

GMO

Content requirement for licence application on closed system operation
(operattional activities)

- Data of workers
- Design of workplace
- Planned projects, and the used biomaterials in these
- Waste treatment
- Applicable precautions, accident-prevention and disaster relief plans
- Environmental impact study

82/2003. Decree of Ministry of Agriculture Appendix 4. 14

GMO

Content requirement for licence application on non-closed system operation

- there exist different regulation on lower and higher order living organism
- plants have special emphasis – they are the most frequently used GMO in non-closed systems

Government regulation No. 148/2003. (IX. 22.) 15

GMO

Content requirement for licence application on non-closed system operation

- General informations (Applicant's data)
- Informations on the genetically modified organism
  - Specifications of the donor or (where applicable) the parents organ.
  - Specifications of the vector
  - Specifications of the modified organsim
- Information connected to the recipient environment and the circumstances of the reception.
- Information on interactions between the GMO and the environment.
  - specifications influencing the survival, the growth and the spread
  - interactions with the environment
- Information on supervision, control, waste treatment, accident prevention plant.

Government regulation No. 148/2003. (IX. 22.) 16

GMO

Application of Transgenic Organism

- GMO microorganism-> closed system
- GMO animals-> closed system
- GMO plants????

- For cultivation (!!!) there are licensed GMO plants in the USA, like:
  - disease resistance cucurbit
  - herbicid resistant soy
  - insect resistant potatoe and cotton
- The cultivation in the EU was not allowed earlier. However the landfil tests are allowed! → Goal is to decrease the technological drawback.
- The Number of landfil tests increases by expontential function.
- >50 type transgenic plants are in application
- Slowly the cultivaton will also allowed…

GMO

Are transgenic plant dangerous?

What are the differences between traditional breeding and application of molecular biology, if both can result the same phenotype?

historically:
Similar genus were crossed, than through more generation they were backcrossed – the exact reasons were unknowkn for changing phenotypes

today:
The changes are well known
Attributions can not only be improved by realted species – there eare unlimited possibilities like genes responsible for frostbite from a North-sea fish.

GMO

What attributes should be brought into transgenic plants?

I. Herbicid tolerancy:

Like selection marker's : since with their applications other plants can be repressed.

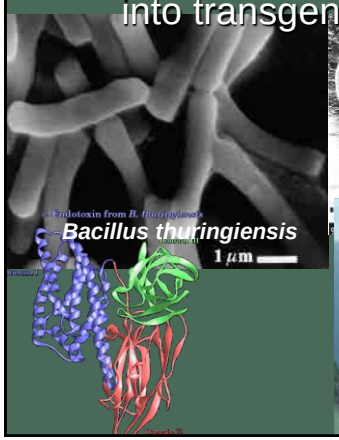
II. Insecticides:

Goal: avoid the usage of toxic chemicals

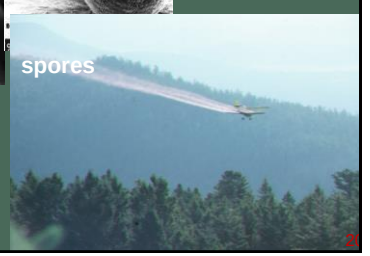
After spyraing, the natural origin (pl. *Bacillus thuringiensis* β-endotoxin, Bt) quickly decomposed. A transgenic plant is able to overproduce→ constant protection

GMO

What attributes should be brought into transgenic plants?



Bt toxins: specificity (they bind to cell-membrane receptors), thus only the malwers will die



GMO

What attributes should be brought into transgenic plants?

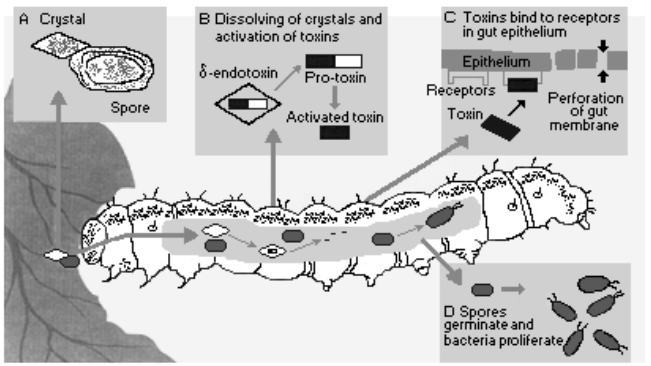


Fig. 1. Mechanism of toxicity of Bt

GMO

What attributes should be brought into transgenic plants?

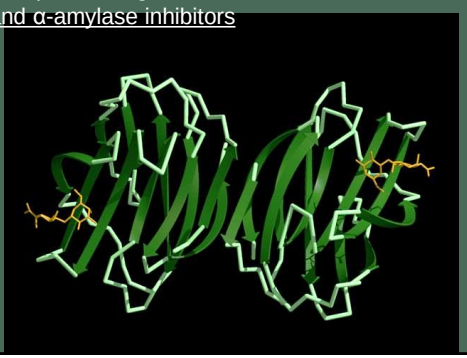
GMO

What attributes should be brought into transgenic plants?

GMO

What attributes should be brought into transgenic plants?

- lectines: epithelial cells of midgut will be damaged. Against lectines from peas and garlic are mammalians not sensitive.
- trypsin and α-amylase inhibitors



GMO

What attributes should be brought into transgenic plants?

III. Disease resistancy:

1. Viral disease: genes of wrong capsid proteins or wrong movement proteins
2. bacterial: cecropins, attacins, magarins, lysosyme
   for Examp.: cecropin B from silkworm (*Hyalophora cecropia*) to cotton

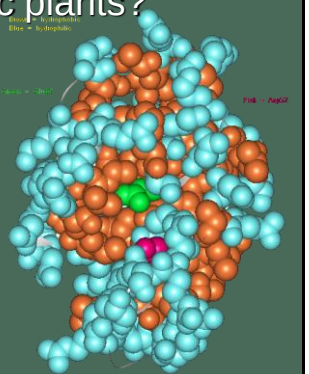
silkworm

Fluoreszcent cecropin (can be in cotton), filament and spores llight -> leakage

GMO

What attributes should be brought into transgenic plants?

For Example: chicken (*Gallus domesticus*) lysosyme into apple



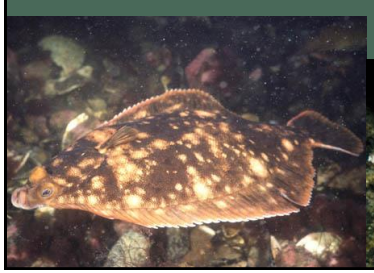
fungal: chitinase, glucanase, phytoalexins

GMO

What attributes should be brought into transgenic plants?

IV. Stress tolerancy:

Against dryness, cold, ozone et.
Like: Genes of *Pseudopleuronectus americanus* (sole) caused cold tolerancy in tomato.



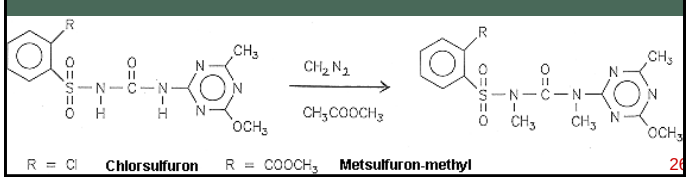
© 1992 Jonathan Bird

GMO

Application risk of transgenic plants

I. Using herbicides:

The wide application of herbicides together with herbicid resistant crops will result the enrichment of toxic herbicides in soil (like sulphonyl-urea etc.)



R = Cl **Chlorsulfuron** R = $COOCH_3$ **Metsulfuron-methyl**

GMO

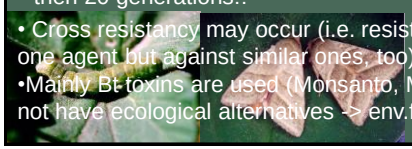
Application risk of transgenic plants

II. Emergence of resistant malware

• The continuous application of pesticides and herbicides will result resistant malwares (i.e. selection preassure – accelerated evolution). like mantis specieses

• This is expected in case of transgenic agents, too.

An Example: The caterpillar of *Heliothis virescens* (=insect) can consume tobacco. In a lab experiment it was verified, that applying high pesticide concentration resistancy occured in less then 20 generations!!



• Cross resistancy may occur (i.e. resistancy not only against one agent but against similar ones, too)..

•Mainly Bt toxins are used (Monsanto, Mycogen), which does not have ecological alternatives -> env.firendly agents will lost.

GMO

Application risk of transgenic plants

GOAL:

To reduce the malwares to an economically acceptable level, beside keep alive the sensitive population too!

Solution:

• resistant and sensitive plants should cultivated togeher (this require reliable farmers)

• the transgene shoud be expressed only in some part of the plant (like fruit, corn, and sprout)

• the production of high toxin concentration required – this kills the partly resistant individuals, and slow down the spread of resistancy in the population.

GMO

Application risk of transgenic plants

III. Competitors and alternatives:

- The weakening of the target malware will be a transient only, becasue it will be substituted by another species!
- The tartget malware may attack another crop.

GMO

Application risk of transgenic plants

IV. Getting out to the mother nature

If the transgenic plant can also survive without human cultivation, it can become later a weed having the new attrubute! Out of the most problematic 18 weeds 11 are also cultivated!!!

V. Hybridization of the cultured and wild plants

For decades, it was examined, how frequently the wild relative plant cross the new crop, decresing with this the productivity.

Recently: the key question is, how frequently the transgenic plant can form hybrides with its wild type relatives i.e. in what extent the transgene can get out?

GMO

Application risk of transgenic plants

IMPORTANT:
Into the nature released transgenes it is impossible to get free!!

Tendency:
more and more different, together not occuring genes are brought into the cultivated crops. If these get out into the nature, can accelerate the evoultion!
This impact can hardly be valued!

GMO

Application risk of transgenic plants

Hybridization with wild species: the transgene get out into the wild type population

- on non-agriculture area fitness improvement: transgeneics shrivel the native species
- landfill (cultivated) area: generation of better viability weeds, against which it is more difficult to fight…

Risk rating of transgenic plants::

1. High
2. Moderate
3. Low

} risk

GMO

Application risk of transgenic plants

High risk level transgenic plants:
•The same species exists in the wild nature
•Create very easily hybrides with the wild type species

For Example: pumpkin, sunflower, radish (pollened by insects) rice (pollened by wind) if wild type variants existed in 500-1000m, hybrides were found!!!

Moderate risk level transgenic plants:
In case of the same genus or same cromosome number some of the formed hybrides can be viable

Low risk level transgenic plants:
The rests (any others)

GMO

Application risk of transgenic plants

Remarks:

• If only a few transgenic hybride is formed, thant this is a strong selection pressure, resulting enrichment of these in the population.

• For now only a few example have been found for transgenic weeds, becasue generally the increse in fitness is too low. But the tendency is to bring always more genes into a host, which increase the possibility for obtaining genetic benefits!

• The attributes, which are not providing evoultionary benefits, will spread less (like drug substances, oil content etc.)

• The attributes, which provide evolutionary benefits (like herbicid resistancy, patogen resistancy, stress tolerancy) will better spread. That is an importan questions, that among a given conditions an attribute will be beneficial or not for the plant?

GMO

Application risk of transgenic plants

Examples:

1. XIX. century, Californian radish + an intrduced weed (*Raphanus rapharistrum*) formed a hybride and spread quickly
2. Johnson grass: that is an interspecies hybride of the most damaging weed of the USA: *Sorghum bicolor* + *Sorghum propinguum* (from Southeast-Asia)

- We have very limited informations on interspecies hybridization. It should be studied case by case, but this would result unlimited experiments…

- Another problem is, that if an artificial crossing is difficult, the natural way result hybrides on the landfills…That means, that we do not have reliable experimental method….

GMO

Application risk of transgenic plants

Thus the emphasize should move from risk assesment to disaster releif.

Some examles to show the social opinion:

GMO

Transgenic plants - Hungary

„Ban now!
Corn-filled bags stood at the entrance to the Prime Minister's Office"

Budapest, 2005. january 18th. – This morning, 15 Greenpeace activists from Hungary and Austria with few bags of corn barricaded the entrance of the Prime Minister's Office, demanding the government to bring in legislation the import ban of genetically modified (GM) maize seeds. "

GMO

Transgenic plants - Hungary

2005 January 20th.

„It was a difficult birth!

The Government had nine months to the imposition of the import ban"

„From Romania into Hungary infiltrate the genetically modified maize seed

2005. march 7th., monday, 01:28:29

The Hungarian Association of Seed Producers warn the Hungarian farmers, that the cheap corn seeds bought in Romanian stores near to the border can be genetically modified, or GM-contaminated."

GMO

Transgenic plants - Hungary

„The security forces dealt with Greenpeace protesters in Warsaw

Népszabadság Online • 2005. february 11th.

Police in Warsaw on Friday removed 30 Greenpeace Environmental Movement's activists from the entrance of Marek Belka polish prime-minister's office after several people chained themselves to the fence, so that they can demand a ban on imports of genetically modified foods."

GMO

Transgenic plants - Hungary

„Failed to Enable the import of genetically modified corn

2004. february 23th. - Agriculture

„Since the Regulatory Committee did not vote for the authorization of genetically modified NK 604 maize varieties EU imports, thus this issue is being returned to the Council."

„However, if the Council adopts the proposal of the committee, the GM maize - which, incidentally, received a favorable evaluation by the European Food Safety Authority (EFSA) - can be imported after the entry into force of the new EU regulation on GM produce."

GMO

A transzgenikus növények - Magyarország

VILÁGGAZDASÁG ONLINE

Economy - Abroad 2008-06-23 11:38:16

Nestlé: The world can not be fed without GM crops

The world's largest food company, Nestle has called on the European policy makers to reconsider their opposition to genetically modified (GM) agricultural crops consideration.

Peter Brabeck, chairman of the company said this is necessary because of the increase in the price of raw materials such essential food items like wheat and rice will be inaccessible to the poorest sections of the world.

Brabeck said to the Financial Times: "... The world today can not be fed without GM crops. We have the tools to make the agriculture sustainable for long term, but for now we do not see the political will "

According to Brabeck, Europe's opposition against biotech crops encouraged African countries for the rejection of genetically modified crops. Peter Mandelson, the EU trade commissioner rejected the argument of the President of Nestlé. "Africa is free to cultivate plants that they want, but a huge part of its agricultural exports directed to the EU, and clearly serve their interests when trying to satisfy the needs of this market" - explains Mandelson.

GMO

The utilization of transgenic microorganism

Because of social rejection:
essence: completely cloed system which prevent the getting out of the GMO

- 90/220 EU directive – emission of GMO's
- 90/219 EU direktíva – application of GMO's in closed system

in year 2002. LXVII., 82/2003. FVM rendelet, 148/2003. Government regulation

Therfore appropriate legal control, technology and its check would be nessecary!

This was not working in Hungary before joining the EU.

GMO

The utilization of transgenic microorganism

A german example: Köln

- 4333000 cittizen, 586 person/km^2
- 5 university, 20 companies working with GMO, 300 closed system enduser
- 2513 biological laboratory, 227 animal-house, 116 GMO exprimental greenhous

Every place is checked by average in every 2-5years wit hair and surface sampling.

(for landfil trials 3 check/yr!!!)

42

GMO

The utilization of transgenic microorganism

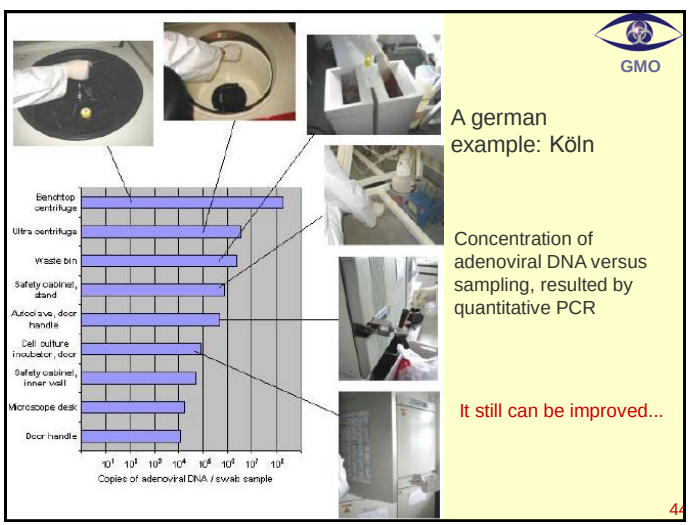
A german example: Köln

3 inspector!!!

	2002		2003	
BSL	1	2	1	2
Closed system GMO utilization.	240	56	249	53
Inspect	123	33	149	23
Sampling		102		84
Non-appropriate	372	120	305	26

Inspects can improve

43



GMO

A german example: Köln

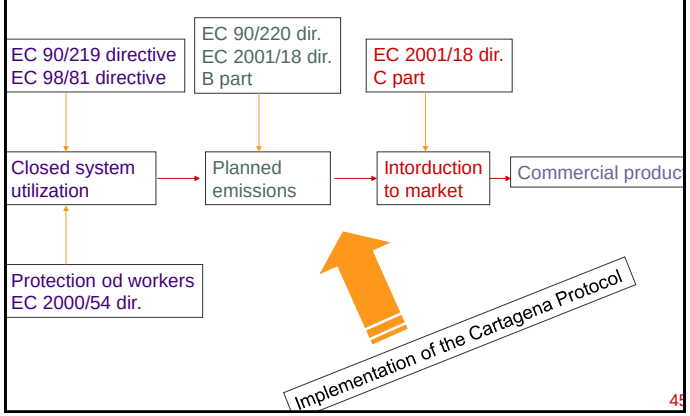
Concentration of adenoviral DNA versus sampling, resulted by quantitative PCR

It still can be improved...

44

GMO

Legal Control



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