Feed from Transgenic Plants in Animal Nutrition

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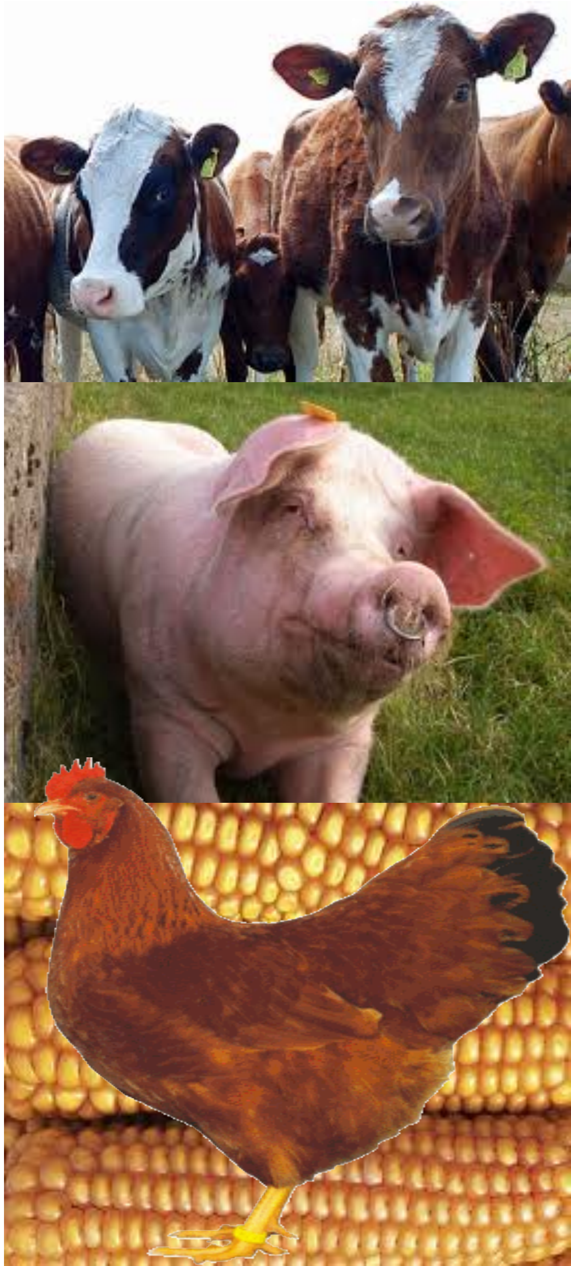
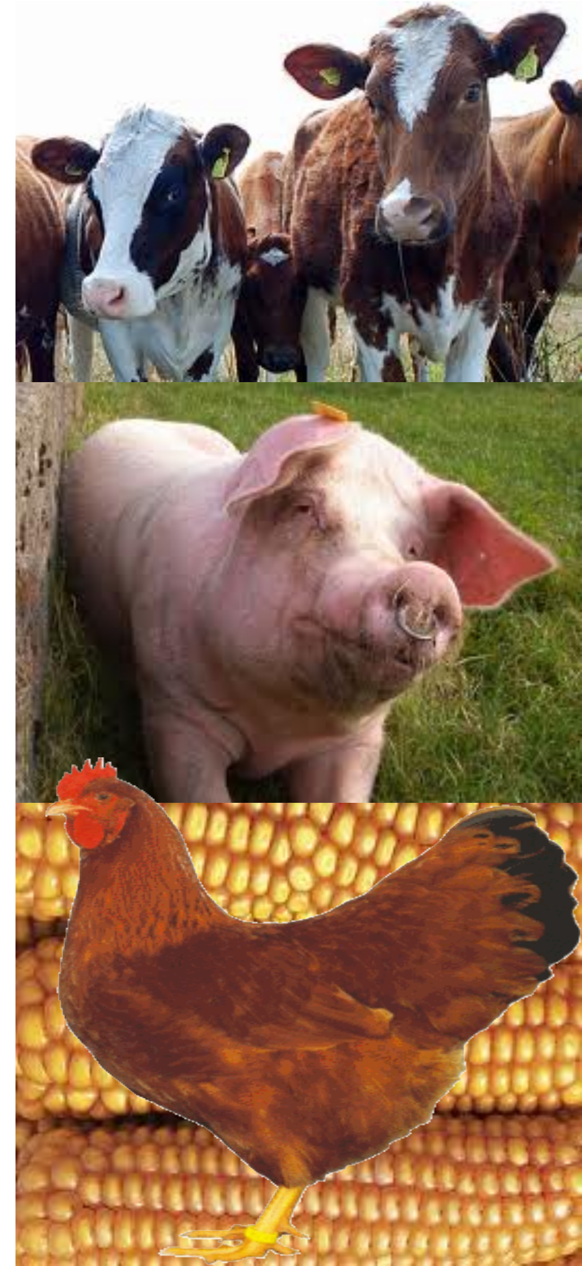


1. Introduction



Global Developments

Population, Need for Food ↑

Resources per People ↓

Emissions ↑

Intake of milk, meat and eggs (kg/person/year) as well as protein of animal origin (min and max-values, global averages; data from 2007; FAO 2009)

Food	Minimum	Average	Maximum
Milk	1.3 (PR Congo)	82.1	367.7 (Sweden)
Meat	3.1 (Bangladesh)	41.2	142.5 (Luxembourg)
Eggs	0.1 (PR Congo)	9.0	20.2 (PR China)
Edible protein of animal origin (g per person per day)	4.0 (Burundi)	23.9	69.0 (USA)

Challenges for animal production or "Livestock's long shadow" (FAO 2006)

Year	Presently	2050	Percent to presently
World population (bill.)	6.5	9.0	138
Meat production (Mio. t)	229	465	203
Milk production (Mio. t)	580	1043	180

Plant Breeding as Starting Point of the Food Chain

Potentials to produce phytogenic biomass and their availability per inhabitant under consideration of the increase of population (Challenges for plant breeders; based on the Royal Society, 2009)

Unlimited resources/Limited Resources

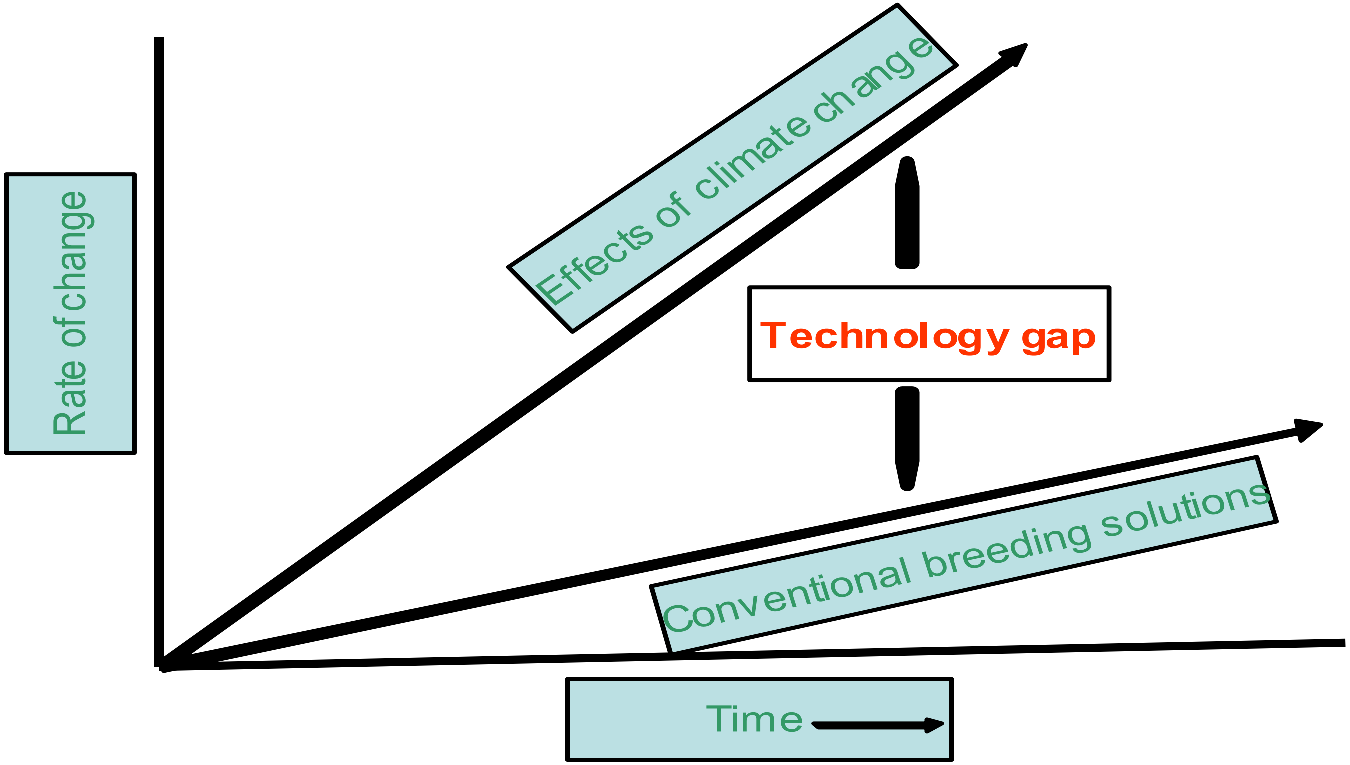
- Sun energy ~
- Plant nutrients in the atmosphere (N_2, CO_2) ~↑

- Agricultural area ↓
- Water ↓
- Fossil energy (Fuel) ↓
- Mineral plant nutrients ↓

- Variation of genetical pool ↑

(↑ Increased, ↓ Decreased, ~ no important influenced)

Keeping pace with climate change
(by Whitford et al. 2010)



Basic wishes to plant breeders incl. plant biotechnology

1. Higher yields and stability through competition for land, climate change, etc.

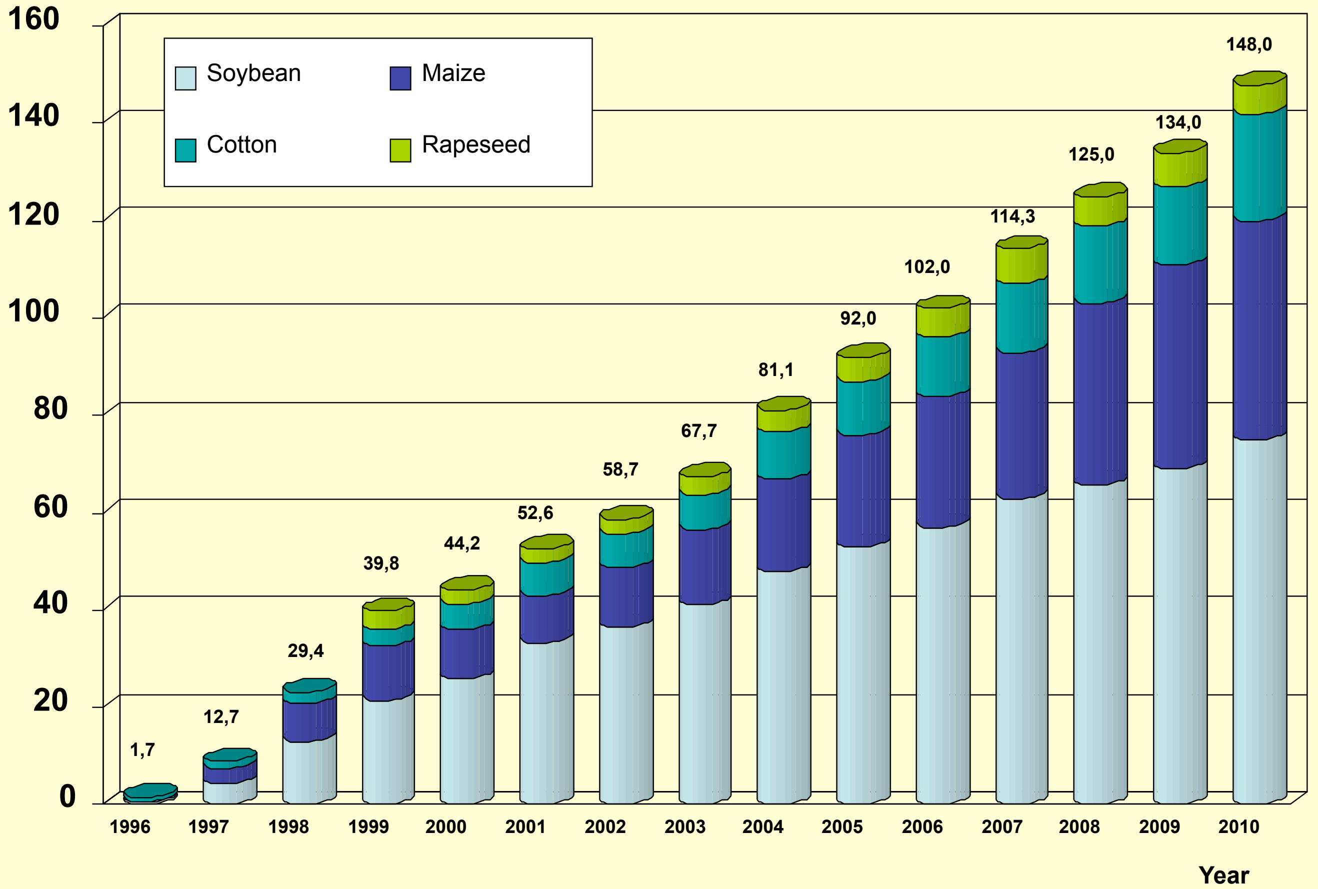
2. More resistent against abiotic and biotic stressors

3. Efficient use of resources with "limited" availability" such as:
   - water
   - crude mineral resources (ie phosphorus)
   - fossil energy (ie N fixation by plants)
   - Arable land

4. More efficient use of "unlimited" ressources (e.g. sun energy, N_2, CO_2, genetic pool)

5. Changes in composition (more valuable/less undesirable substances)

Global area of transgenic crops (in mio. ha; James 2011)



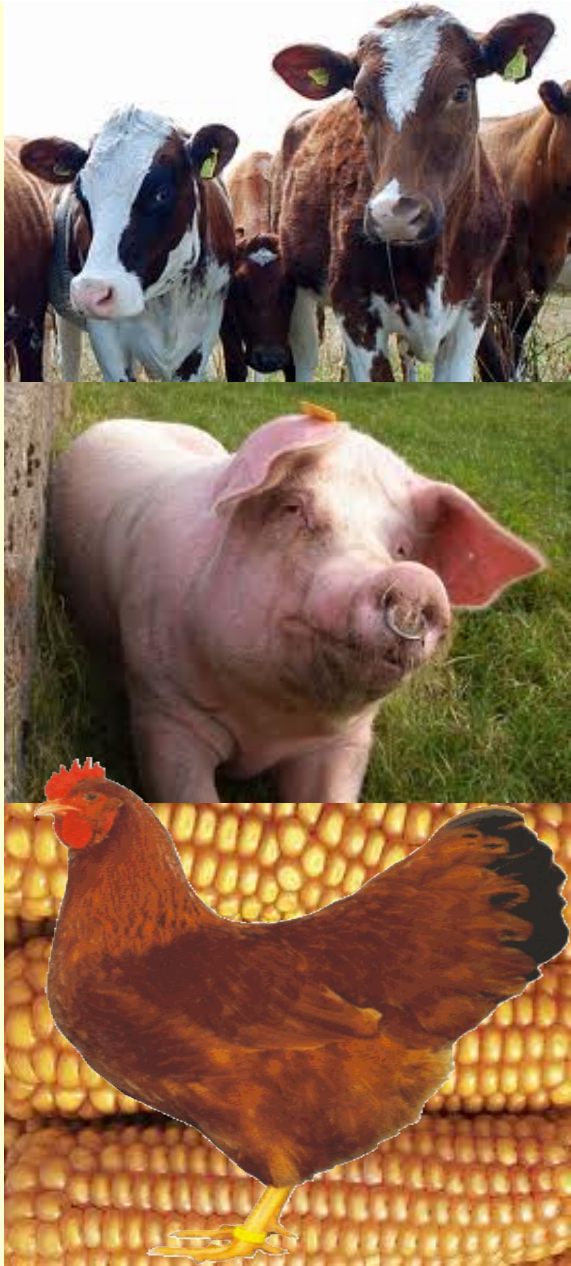
Events in commercial GM - crops worldwide, by trait (Stein and Rodriguez-Cerzo, 2009)

Trait category	Commercial in 2008
Insect resistance	21
Herbicide tolerance	10
Crop composition	0
Virus resistance	5
Abiotic stress tolerance	0
Disease resistance	0
Nematode resistance	0
Fungus resistance	0
Other	2

Important food/feed from GM-plants and estimated portion used as food or feed (own estimation)

GM-Plant	Food	%	Feed	%
Soybean	Oil, Proteins	25	Soybean (extracted oil) meal, Full fat soybean	75
Maize	Starch, maize meal, Oil	15	Maize, Oil, DDGS, Gluten feed, Silage, Straw,	85
Rapeseed	Oil	25	Rape seed (extracted oil) meal, Rapeseed expeller/cake, Fullfat rapeseed	75
Cotton	Oil	15	Cotton seed (extracted oil) meal, Expeller	85

2. Definitions and Questions to Nutritionists



Nutritional view of GM-Crops
- Definitions -

GMP of the 1st generation

- Plants with agrotechnical traits (input traits)
- Without substantial changes in composition/nutritive value
- Substantial equivalent
- Examples:

  Bt-plants (corn, cotton), RR-plants (soybean), PAT-plants (corn, roots) etc.

GMP of the 2nd generation

- Plants with output traits
- With substantial changes in composition/nutritive value
- Not substantial equivalent
- Examples:

  Golden rice, low phytate corn, changes in fatty acids (e.g. MON 87769) or amino acids pattern etc.

Substantial Equivalence (S.E.) → Quo vadis?

S.E. (OECD,1993) embodies the concept that if a new food/feed is found to be substantially equivalent to an existing food/feed, it can be treated in the same manner with respect to safety as its traditional counterpart.

Problems

- **Coarse frame work for evaluation; limited safety and nutritional assessment**
- **What means traditional counterpart (isogenic plants or local average)**
- **Irrational if changes in composition (e.g. lower content in mycotoxins, GMP of the 2nd generation)**

Proposal

Various compartments should be considered as parts of S.E. as

- **Chemical/analytical equivalence**
- **Nutritional equivalence**
- **Safety equivalence**
- **Exposure equivalence**

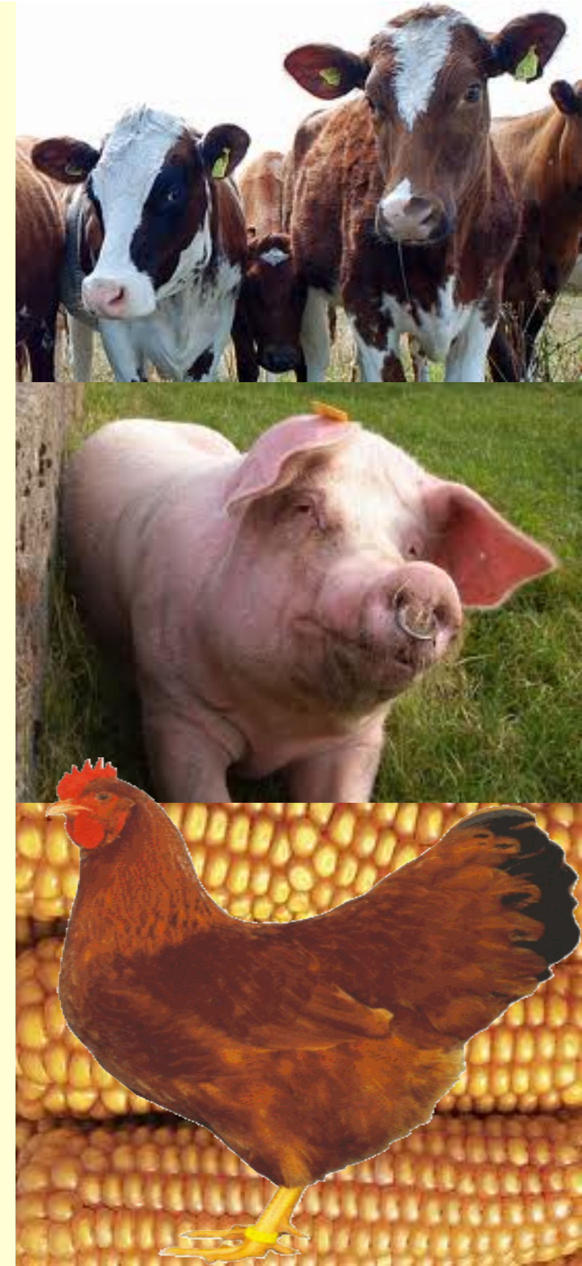
Questions to animal nutritionists

- **Nutritional and safety assessment of feed and food of the 1st generation of GMP**
- **Nutritional and safety assessment of feed and food of the 2nd generation of GMP**
- **Influence of GM-feed on animal health and quality of food of animal origin**
- **Studies on the degradation of newly expressed protein, foreign DNA, “unintended effects” etc.**

Examples for guidelines for nutritional and safety assessment of food and feed from GMP

ILSI (2003) EFSA (2004)	Assessment of GMP of the 1st generation (input traits)
ILSI (2007) EFSA (2008)	Assessment of GMP of the 2nd generation (output traits)
New activities of the EFSA (2011)	Guidance Doc. for GM-Animals, 90-day toxicity study on whole food/feed

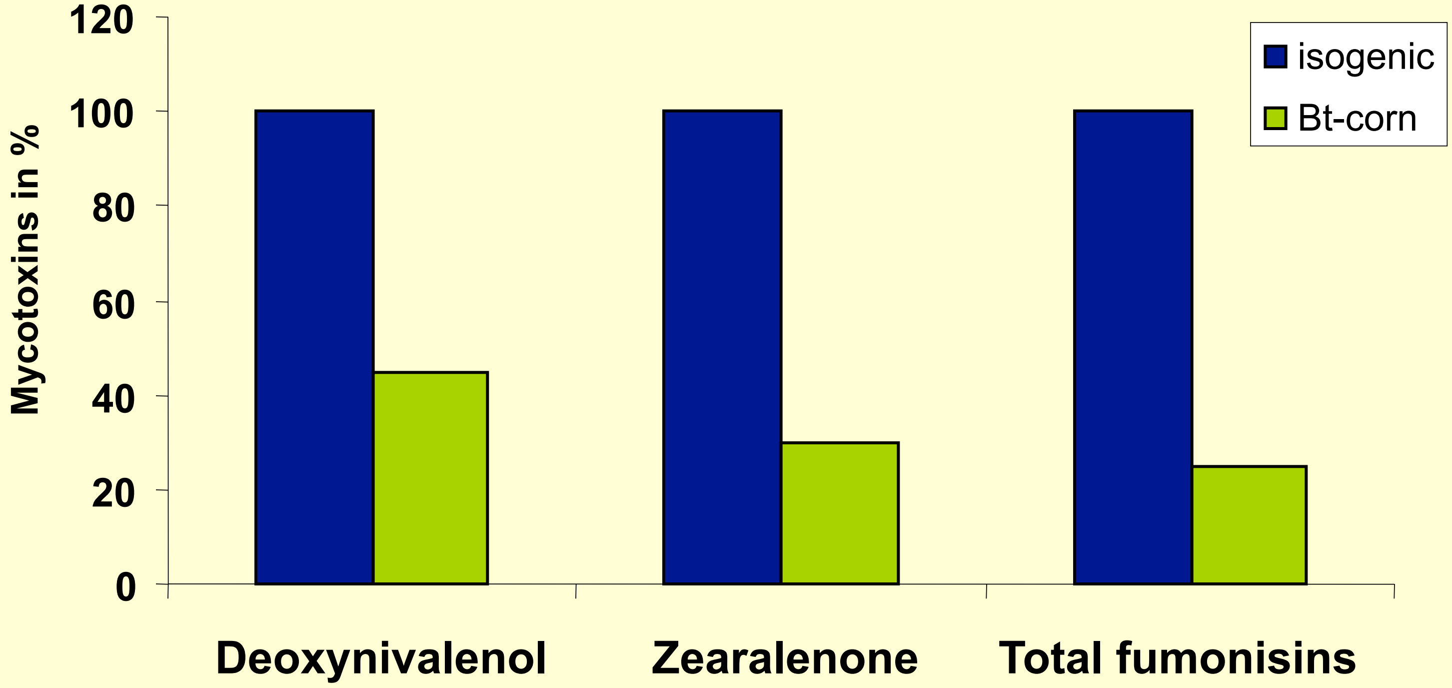
3. Experiments with Food Producing Animals



Recommendations for compositional Analysis of GMP, isogenic counterparts and commercial varieties for nonruminants(see OECD 2001-2005; ILSI 2007)

Crops/Grains/ Coproducts	Livestock Type	Analyte
Grain: maize, wheat, barley	Non-ruminants	DM, CP, EE, ADF, NDF, Ca, P, Mg, K, S, Na, Cl, Fe, Cu, Mn, Zn, ash, starch, lysine, methionine, cystine, threonine, trytophan, isoleucine, arginine, phenylalanine, histidine, leucine, tyrosine, valine, fatty acids, vitamins
Oilseed meals: soybean, linseed, cottonseed, canola meal, full-fat oilseeds	Non-ruminants	DM, CP, EE, ADF, NDF, Ca, P, Mg, K, S, Na, Cl, Fe, Cu, Mn, Zn, ash, starch, lysine, methionine, cystine, threonine, tryptophane, ispleucine, arginine, phenylalanine, histidine, leucine, tyrosine, valine, fatty acids, vitamins

Mycotoxins in isogenic (100 %) and Bt-corn (% of isogenic corn; data from some references)



Objectives for Animal Feeding Trials (in vivo) with GM-Products

- Do we need additional information to compositional analysis and in silico, in vitro and/or in situ studies?
- What are unindented effects and do we expect such effects?
- Do we expect long term effects (incl. effects on health, fertility etc.)?
- Do we expect effects on product quality (food of animal origin)?
- Do we need additional information from GMP with output traits (e.g. bioavailability of nutrients) or GM-animals (e.g. new energy and nutrient requirements)?
- Can we expect innovations for safety and nutritional research (feed science)?
- Are animal studies important/necessary from the view of public concerns and/or may the studies contribute to more public acceptance?

Present recommendation: Case by case decision

Types of studies with target animals

- **Metabolism studies**
  (Digestibility, Bioavailability etc.; see EFSA 2008)
- **Tolerance studies**
  (studies concerning safety; see EFSA 2008)
- **Efficacy studies (see EFSA 2008)**
- **Long term studies (see Review by Chelsea et al. 2011)**
- **Multigeneration studies (see Chelsea et al. 2011)**
- **Studies with GM-animals (see EFSA 2011)**

Important types of feeding studies and animals recommended

Type of studies	Lab. Animals	Target Animals
Testing of single substances (28 day study)	X	
90-day rodent feeding study	X	
Long-term feeding study	X	X
Multigeneration feeding study	X	X
Determination of digestibility/availability	X	X
Efficience study		X
Tolerance study		X
Studies with GM-animals		X

Recommendation by ILSI (2007) for performance studies

…Most studies should have **the test grain transgen, its near isogenic counterpart (control)**, and, preferably, **four or more conventional reference varieties** to help explain any unexpected differences or confirm any expected differences observed between the test and the control…

Experimental design

1. Transgenic hybrid
2. Isogen counterpart
3. Some (at least 3) conventional (commercial, non-transgenic) reference varieties

Effect of the maize event DAS-59122-7 (53 to 70% maize in the diet) on growth performance and organ weight of broilers in comparison to the near isogenic control and three non-transgenic conventional hybrids (120 broiler per treatment, 42 days, McNaughton et al., 2007)

Criteria	Control	DAS-59122-7	Confidence interval (95%)
Final weight (g/animal)	1918	1916	1675 - 2144
Feed: gain (g/g)	1.88	1.87	1.70 - 2.03
Relative weights of some organs (g/kg body weight) Kidney ♂ ♀	 20 20	 20 21	 8.5 – 33.2 8.2 – 33.2
Liver ♂ ♀	 35 34[a]	 36 37[b]	 20.5 – 50.6 19.5 – 51.0
Post-chill carcass (g/kg body weight) ♂ ♀	 708 705	 713 707	 626 – 792 622 - 791

[a, b] Different letter in one line show sign. differences ($p < 0.05$)

What means ????

STATISTICAL SIGNIFICANCE and BIOLOGICAL RELEVANCE? (EFSA 2011)

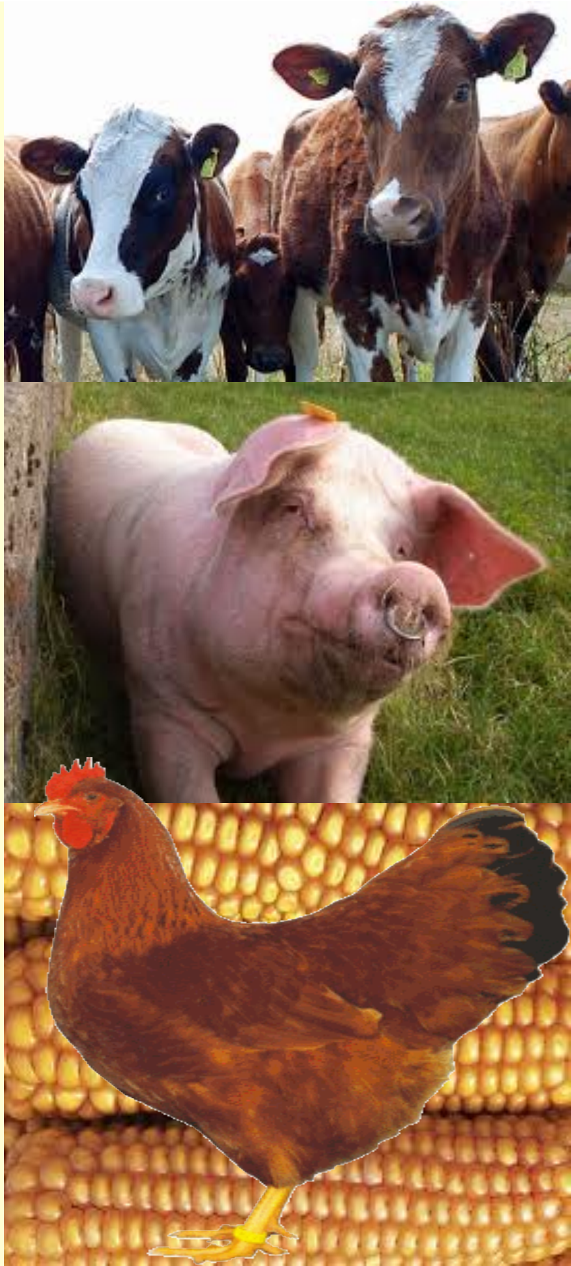
Less emphasis should be placed upon reporting of statistical significance and more on statistical estimation and associated **interval estimation (e.g. Confidence Interval).**

Endpoints of Feeding Studies

- Feed intake, body weight and weight gain, yield in eggs, feed conversion rate (FCR)
- Animal behavior, health, mortality, fertility
- Physiological parameters in body samples
- Weight of organs and tissues
- Chemical composition of food of animal origin (e.g. eggs, tissues, organs)

3.1. Results from Feeding Studies with GMP with Input Traits

(1st Generation)



Summary of published data to compare feeds from GM plants of the first generation (with input traits) with their isogenic counterparts (Summary from 2010)

Animal (Species/ categories)	Number of experiments	Nutritional assessment
Ruminants		No unintended effects in composition and contamination (except lower mycotoxins concentrations in Bt plants)
Dairy cows	23	
Beef cattle	14	
Others	10	
Pigs	21	
Poultry		No biological relevant effects on digestibility and animal health as well as no unintended effects on performances of animals and composition of food of animal origin
Laying hens	12	
Broilers	48	
Others	1	
Others (Fish, rabbits etc.)	8	

Performance and some metabolic parameters of the 1st and 2nd lactation of a long-term feeding study with dairy cows (n=18 per treatment, 25 months with Bt-maize (MON 810, 63 % of roughage, 41 % of concentrate from maize, Steinke et al. 2009)[1)]

Lactation of experiment	1st		P-level	2nd		P-level
	isogenic	transgenic		isogenic	transgenic	
Dry matter intake (kg/d)	18.7	18.9	0.532	21.0	20.4	0.080
Milk yield (kg/d)	23.9	23.7	0.566	29.2	28.8	0.419
Milk fat (%)	3.95	4.03	0.015	3.75	3.86	0.055
Milk protein (%)	3.62	3.71	<0.001	3.59	3.56	0.299
NEFA (µmol/l)	287	281	0.991	292	290	0.988
BHBA (mmol/l)	0.46	0.44	0.107	0.50	0.49	0.304
AST (U/l)	92.6	89.8	0.263	94.3	88.8	0.177
GLDH (U/l)	19.5	19.1	0.922	13.8	16.1	0.178
γ-GT (U/l)	23.2	23.9	0.426	23.5	23.9	0.575

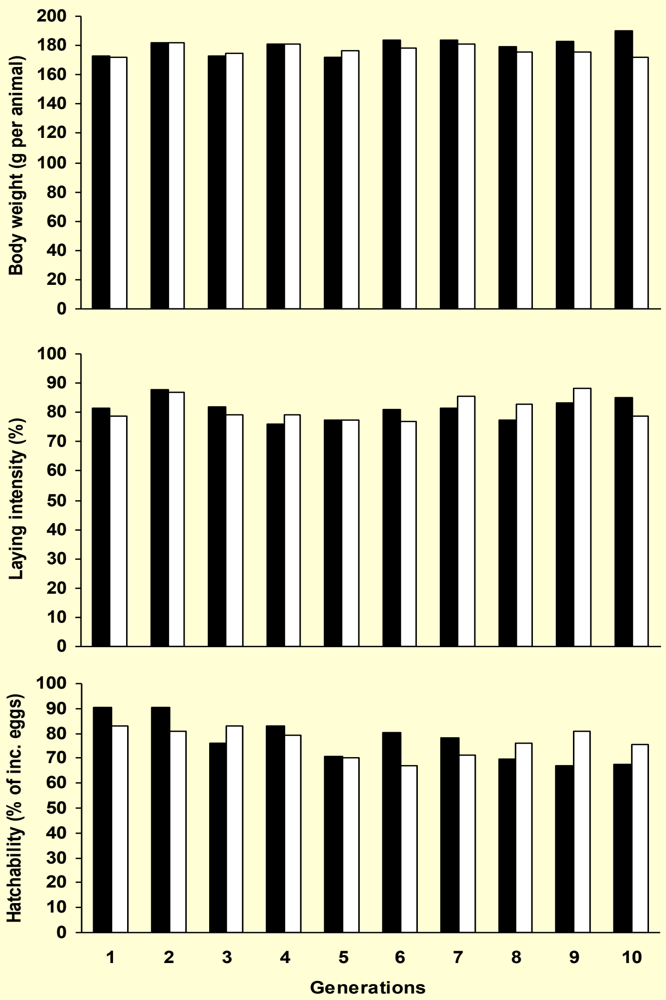
[1)] No fragments of Cry1Ab-DNA in blood, milk, feces and urine of cows; traces of Cry1Ab protein were detected in feces, but not in blood, milk and urine (Gürtler et al. 2009)

(A) Body weight of female quails (age: 6 weeks), (B) laying intensity and (C) hatchability of quails fed with isogenic (■) and transgenic (Bt, □) corn in a 10 generations experiment

A

B

C

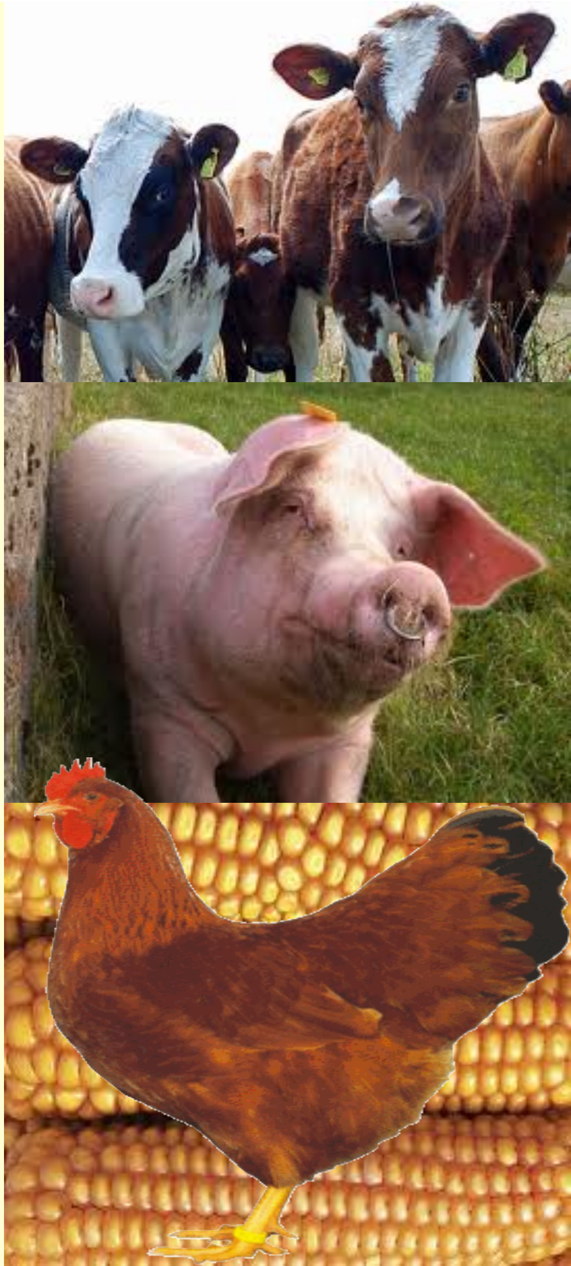


Overall means (Range of generations)

	Isogenic	Transgenic
A	180.1 (172.0 – 190.1)	176.9 (171.9 – 181.7)
B	81.3 (75.9 – 87.8)	81.4 (77.1 – 88.4)
C	77.4 (66.8 – 90.5)	76.7 (67.0 – 83.2)

3.2. Nutritional and Safety Assessment of GMP with Output Traits

(2nd Generation)



GM - crops with output traits (GMP of the second generation)

- Increased content of desirable/valuable substances
  - Nutrient precursors (e. g. β-carotene)
  - Nutrients (amino acids, fatty acids, vitamins, minerals etc.)
  - Substances which may improve nutrient digestibility (e. g. enzymes)
  - Substances with surplus effects (e. g. prebiotics)
  - Improvement of sensoric properties/ palatability (e. g. essential oils, aromas)
- Decreased content of undesirable substances
  - Inhibiting substances (e. g. lignin, phytate)
  - Toxic substances (e. g. alkaloids, glucosinolates, mycotoxins)

Examples of GMP with improved characteristics intended to provide nutritional benefits (by EFSA 2008)

Plant/species	Altered characteristic	Transgene/Mechanism
Maize	Improved amino acid profile ↑ Vitamin C↑ Bioavailable iron ↑ Fumonisin ↓	Various enzymes Dehydroascorbate reductase Ferritin and Phytase De-esterase and de-aminase
Potatoes	Starch ↑ Solanine ↓	ADP glucose pyrophosphorylase Antisensesterol glycotransferase
Rapeseed	Vitamin E ↑ ß-Carotene ↑ Linoleic acids ↑	Gamma-Tocopheryltransferase Phytoene-Synthase Various desaturase
Rice	ß-Carotene ↑ Iron ↑	Phytoene-Synthase and –desaturase, Lycopene cyclase Ferritin, Metallothionein, Phytase
Soybean	Oleic acid ↑ Stearidonic acid ↑	Suppression of desaturase Various desaturase

Pro and Contra of substantial changes in plant composition

PRO	CONTRA
Advantages for human nutrition (meet requirements; e.g. Amino acids, Fatty acids, Minerals, Vitamins etc.)	Many feed additives for animal nutrition are available on the market
	Plant breeding needs long time
Improvement of properties of food/feed	High amounts of food/feed may be necessary to meet requirements

Examples for nutritional assessment of a GMP of the 2nd generation (GM-plant with output traits; e.g. higher concentration of the vitamin A precursor ß-carotene; by EFSA 2008)

Groups	Composition of diets	Measurements: endpoints
1	Balanced diet with typical amounts of the isogenic counterparts (unsupplemented control)	Depend on genetical modification of plants, e.g.:
2	Balanced diet with adequate amounts of the transgenic counterpart (e.g. rich in ß-carotene)	- Concentration of specific substance(s) in target organ (e.g. vit. A in the liver)
3	Diet of Group 1 with ß-carotene supplementation adequate to Group 2	- Further metabolic parameters such as depots in further organs or tissues, activities of enzymes and hormones
4	Diet of Group 1 with vitamin A supplementation adequate to expected ß-carotene conversion into vitamin A	

Experimental design to determine the conversion of β-carotene into vitamin A in maize

(60 % of diet, Mongolian gerbils, n = 10, Depletion period: 4 weeks, Feeding: 8 weeks, Howe and Tanumihardjo, 2006)

	Unsupplemented control (Maize poor in carotene)	Carotene rich maize	Control + β-carotene	Control + vitamin A
β-Carotene (nmol/g)	0	8.8	8.8	4.4
Theoretical retinol intake (nmol/d)	0	106	106	106
Retinol in serum (µmol/l)	1.23 ± 0.20	1.25 ± 0.22	1.23 ± 0.20	1.22 ± 0.16
Retinol in liver (µmol/g)	0.10^{a} ± 0.04	0.25^{b} ± 0.15	0.25^{b} ± 0.08	0.56^{c} ± 0.15

$^{a, b, c}$ Means with different letters differ ($p < 0.05$)

Proposal to assess the effects of inhibitors of nutrient bioavailability (e. g., phytate)

Groups[1]	Diet composition	Measurements
1	Balanced diet including typical levels of isogenic counterpart, ad lib. feeding	Depends on the claim of genetic modification: - Digestibility of inhibited nutrient - Growing experiment with target animals - Concentration of inhibited nutrient in indicator organs
2	Diets of Group 1 plus inhibited nutrient (e.g., P), ad lib. feeding	
3	Balanced diet including transgenic counterpart in adequate levels to Group 1 (e.g., low phytate crop)	
4	Diets of Group 3 plus inhibited nutrient of Group 2	

[1] Four or more groups with commercial isogenic plants

Conventional and low-phytate maize (78.5 % of the mixture) in the feed of fattening pigs (from Spencer et al., 2000)

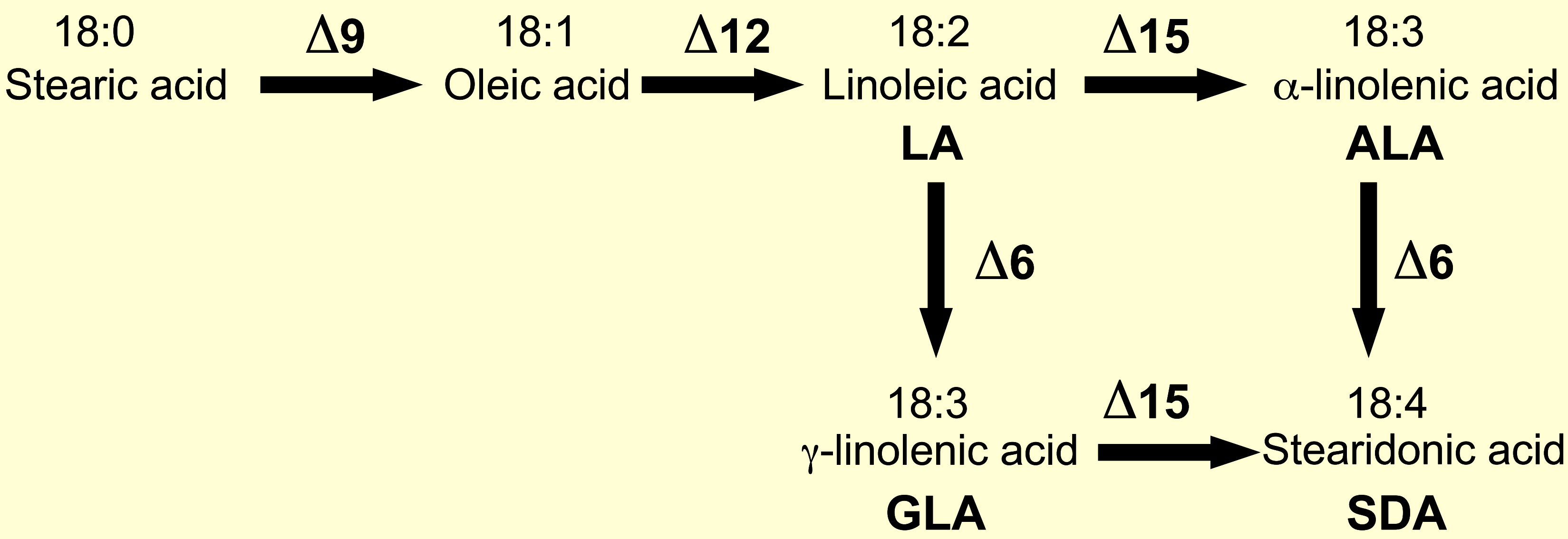
	Control (0.3 g of available P per kg)		Low-phytate maize (1.7 g of available P per g)	
Inorganic P supplement	-	+	-	+
P content (g/kg)				
29 - 73 kg live weight	3.4	5.4 [1)]	3.4	5.4 [1)]
73 - 112 kg live weight	3.2	4.7 [2)]	3.2	4.7 [2)]
Feed intake (kg/d)	2.23 [a]	2.50 [b]	2.53 [b]	2.51 [b]
Live weight gain (g/d)	730 [a]	870 [b]	900 [b]	880 [b]
Feed per gain (kg/kg)	3.05 [a]	2.87 [b]	2.81 [b]	2.85 [b]
P excreted (g/kg)	4.6 [a]	8.9 [c]	3.8 [b]	8.8 [c]
Strength (4th metacarpal bone, kg)	79.4 [a]	138.5 [bc]	132.2 [b]	153.9 [d]
Ash content (% in 4th metacarpal bone)	53.5 [a]	60.1 [bc]	59.3 [b]	61.2 [c]

[a, b, c, d] Different letters in one line indicate significant differences ($p < 0.05$)

[1)] +2.0 g P/kg [2)] +1.5 g P/kg

Newly Expressed Fatty Acids

Fatty acid biosynthesis in plants and the new introduced Changes to produce Stearidonic acid (C18:4 n-3) and the effects of various desaturases (by Ursin 2003 and Whelan 2009)



C18-Fatty acids (in %) in Soybean oil (SDA-oil) of isogenic and transgenic Soybeans (MON 87769)

	Control	MON 87769
C18:0	5	4
C18:1	25	20
C18:2	50	25
C18:3	8	10
C18:4	0	25 (16,8 – 33,9)
Traces of tFA	0	0,3-0,7

(C18c6,c9,c12,t15 and C18c9,c12,t15)

C18:4n-3 (stearidonic acis) soybean oil to broilers (Rymer et al. 2011)

- Ca. 24% SDA in soybean oil
- 45 (grower) and 50g/kg SDA-oil (finisher) in broiler diets compared with normal soybean oil
- No sign. influence on FA, WG and FCR
- Increase of C18:4n-3, C20:5n-3 and C22:5n-3 and 6n-3 in breast and leg meat and in skin

Concentration of some n-3 fatty acids (mg/100g fresh tissue) in body samples (Rymer et al. 2011)

Sample	Control	+ 45 or 50g SDA-oil per kg
Breast meat		
C18:4n-3	3	231
C20:5n-3	12	28
C22:6n-3	7	14
Leg meat		
C18:4n-3	10	442
C20:5n-3	5	53
C22:6n-3	8	21
Skin		
C18:4n-3	111	3673
C20:5n-3	31	317
C22:6n-3	21	78

Degradation of tDNA and newly expressed proteins

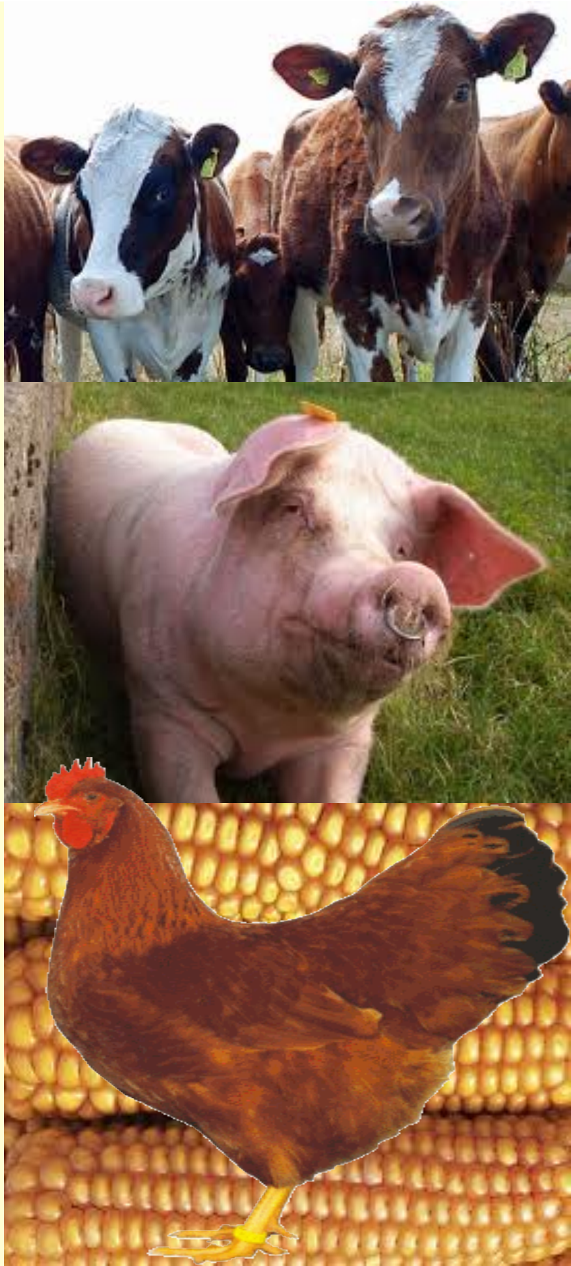
Conclusions: Degradation of tDNA

- **DNA is a permanent part of food/feed** (daily intake: men: 0.1 – 1 g; pig: 0.5-4 g; cow: 40-60 g)
- tDNA intake amounted to ~0.005% of total DNA-intake, if 50 % of diet come from GM-crops
- DNA is mostly **degraded during conservation** (silage making) and **industrial processing** as well as in the **digestive tract** (pH, enzymes)
- **Small fragments of DNA may pass through the mucosa** and may be detected in some body tissues (esp. leucocytes, liver, spleen)
- There exist no data, that tDNA is characterized by another **behaviour as native plant-DNA** during feed treatment and in the animals

Conclusions: Degradation of newly expressed Proteins

- In the ruminants feed protein are mostly degraded in the rumen and microbial protein and by-pass **protein is degraded by enzymes** in the smaller intestine, similar to nonruminants
- The chemical and physiological properties (including microbial and enzymatic degradation) of novel proteins have been intensively tested
- Intact novel proteins were not detected outside of the digestive tract in target animals
- There is **no advice, that newly expressed proteins are characterized by other chemical/physical properties** as native protein

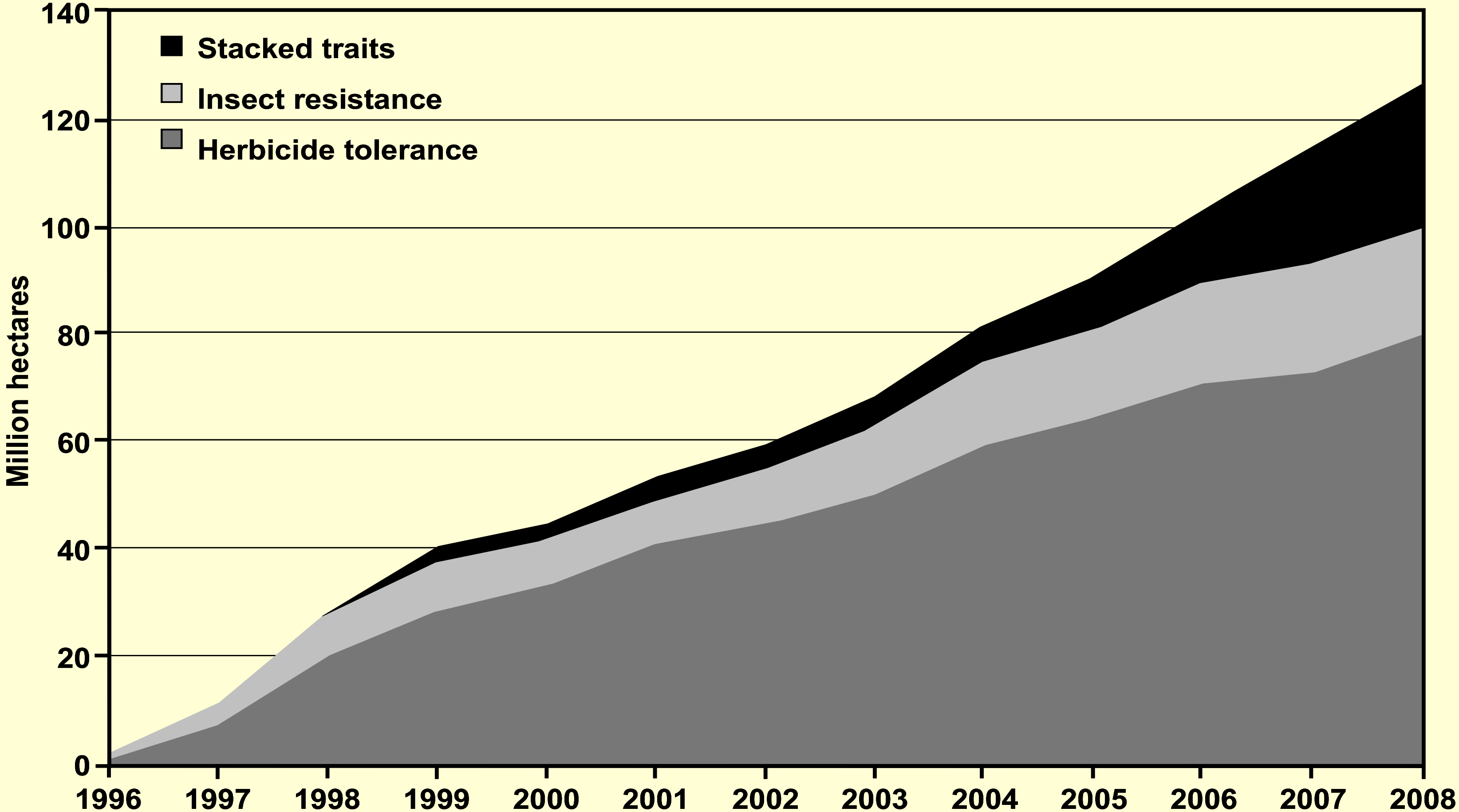
4. New Developments/ Challenges



Future tendencies
(EFSA 2009, Stein and Rodriguez-Cerzo, 2009)

- **Combination** of some stacks in one hybrid
- **Improvement** of nutritional properties (e.g. amino acids, fatty acids, vitamins, minerals, enzymes, lower content of undesirable components)
- **More efficient** use of limited resources (e.g. water, fuel, arable land, N); Tolerance against biotic and abiotic stressors
- **GM-animals** (e.g. phytase pigs/chicken; Golovan et al. 2001; Cho et al. 2006)

Global area cultivated with the main GM traits (by Stein and Rodriguez-Cerezo 2009)



Source: Based on data from James (2008 & previous years)

Events in commercial GM - crops and pipelines worldwide, by trait (Stein and Rodriguez-Cerzo, 2009)

Trait category	Commercial in 2008	Total by 2015
Insect resistance	21	57
Herbicide tolerance	10	32
Crop composition	0	16
Virus resistance	5	10
Abiotic stress tolerance	0	5
Disease resistance	0	4
Nematode resistance	0	1
Fungus resistance	0	1
Other	2	13

Possible Challenges as Climate Change-Related Problems (by Whitford et al. 2011)

- Adaption to greater extremes in climate conditions and higher temperatures (**Flowering time, Heat tolerance**)
- Water supply limited or more variable (**Drought tolerance**)
- Increasing soil salination (**Salt tolerance**)
- **More efficient** use of plant nutrients (eg. N, CO_2)
- Higher disease **infection** and pest **infestations**

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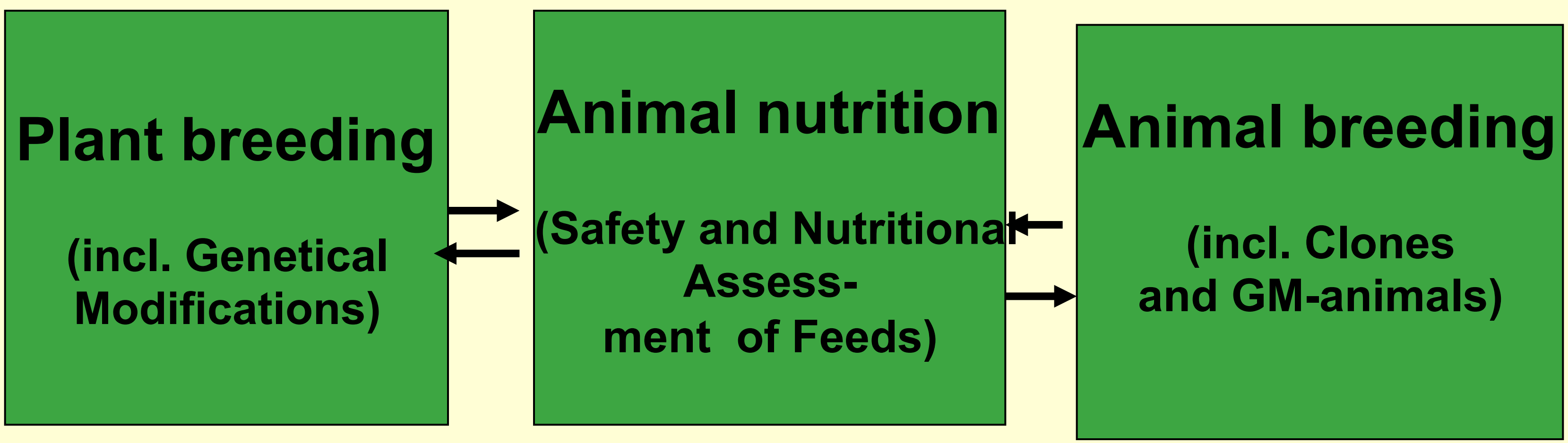
P-digestibility (%) of non-transgenic and transgenic pigs using soybean meal as the sole source of P (Golovan et al. 2001)

Pigs (Body weight)	Non-transgenic	Transgenic (environment pig)
Weaning (6-15 kg)	48.5 ± 5.4 (n = 16)	87.9 ± 3.4 (n = 14)
Growing-finishing (20-65 kg)	51.9 ± 10.3 (n = 16)	98.8 ± 3.4 (n = 14)

5. Conclusions and Summary

Animal nutrition
(Safety and nutritional assesment of food/feed)
between plant and animal breeding



Open questions

- Do we need more feeding trials with stacked events (more tDNA, more transgenic protein)?
- Do we need more feeding trials with GM-plants, which use resources more efficient (e.g. water, abiotic stress)?
- Do we need adequate studies with plants (feed) from traditional breeding?
- Which types of studies do we need with GM-animals?

Assessment of present modifications of plants from the view of food safety and food security (sustainability

Objectives	Present significance	Contributions to	
		Food safety	Global food security
More tolerant against herbicides	↑↑↑	(↑)	↑
Mores resistant against insects etc.	↑↑↑	↑↑	↑
More valuable ingredients	↑	~	↑
Less undesirable ingredients	(↑)	↑↑	↑
More efficient use of resources (water etc.)	(↑)	↑	↑↑↑

↑↑↑ extremely high ↑↑ very high ↑ high ~ not important

Summary

- Up to now more than 1 Billion ha of GM-crops have been cultivated allover the world
- Most animal studies were done with GM-crops of the 1st generation (with input traits)
- No unintended effects in composition (except lower mycotoxins), nutrition and safety were registered in about 150 studies with food producing animals (target animals)
- tDNA and newly expressed proteins in GM-crops show similar properties during processing and in animals as “normal” plant-DNA and proteins
- Other experimental designs are recommended for nutritional and safety assessment of feeds from GM-crops of the 2nd generation (with output traits) and of GM-animals
- Furthermore case by case studies seem to be necessary to answer open questions, more groups with isogenic counterparts should be included
- Feeding studies with food producing animals should be also used for safety assessment

Many Thanks for Your Attention!

Reserve

- Importance of animal feeding studies for improvement of public acceptance of GMP or GM feed/food (also in the case of substantial eqivalence)?

Important conclusions from an Online Survey on animal and human health after long - term feeding of GMP (BVL; unpublished 2009)

- Potential long - term effects were expected in relation to allergenicity
- Other adverse long - term effects were assessed as negligible
- Methodical improvement of the risk assessment procedure
  - Higher number of replications
  - Additional control groups to demonstrate the biological range of measured parameters

Comments to some studies with certain disturbances after feeding of GM-crops (I)

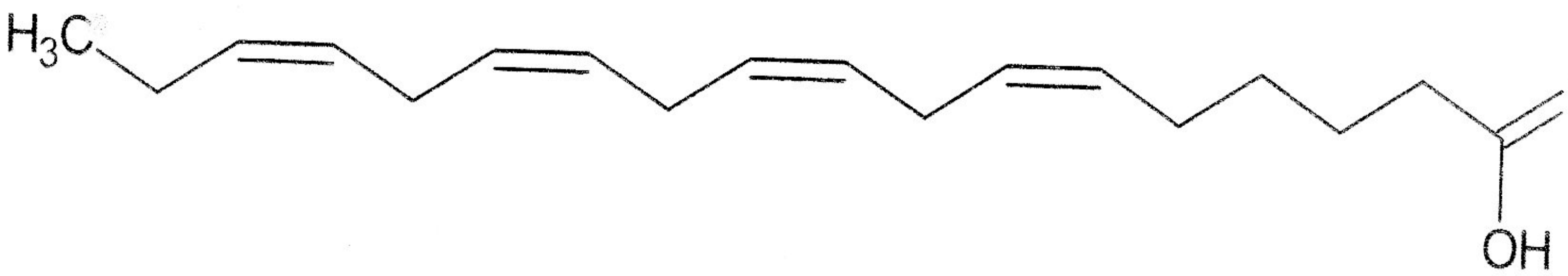
Authors	Study	Results	Comments
Nordlee et al., 1996	Transgen of Paranut in soybean and corn	Allergenic reactions in man	Scientific study, no practical relevance
Ewen and Pusztai 1999	Lectin potatoes to rats	Influence on intestinal tract, disturbance of reproduction	Scientific study, no practical relevance
Maletesta et al., 2002, 2003	RR soybean to mice: comparison with wild variety	Increased cell nucleus in liver and pancreas	Methodical weaknesses, comparison with wild variety, What is normal? Relevance of results?
Hemre et al., 2005	RR soybean to salmon	Increase of spleen, influence on spleen functions, more smaller erythrocytes	What is normal? Repetition of study
Mc Naughton et al., 2007	Maize event DAS-59122-7 in broilers	No differences, but liver of female rats was 3 g/kg heavier ($p<0.05$)	Values in physiological range; overestimation of data; What is normal? Statistical significance, but biological not relevant.
Poulsen et al., 2007a,b	Feeding transgenic Lectin-rice to rats (Spiking of feed)	Disturbances in development and fertility	Scientific study, no practical relevance

Authors	Study	Results	Comments
Seralini et al., 2007	New analysis of the rat feeding study by the notifier (Monsanto) with MON 863	Some differences in liver and kidney parameters	Critical analysis of the 90-days rat study, differences not directed, statistical significant, but biological not relevant (see Doull et al.,, 2007)
Scholtz et al., 2008	Feeding of 50% Bt-corn in longterm study in qualils	Differences in some enzymatic activities between both groups	Physiological relevance, what is normal? Other results after repetition of study
Surov, 2009	3 generations study with hamsters, added GM-soybean to the diet, 5 pairs per treatment	Lower reproduction of hamsters fed with GM soybean	Presently no scientific publication; only preliminary report, scientific assessment not possible
Velimirov et al., 2008	Long term reproduction studies in mice fed transgenic corn NK603xMON810	Some disturbances in reproduction of mice	Withdraw by the Austrian officials (March 2010)
De Vendomois et al., 2009	Reanalysis of 90 day rat feeding studies with corn varieties MON 863, MON 810, NK 603	More significant differences than reportet by the notfier (Monsanto)	Weaknesses in the statistical methods used for reanalysis (see Doull et al., 2007)

Contributions of Plant Breeding to Global Food Security

- Breeding of low input plant varieties with high and stable yields with traditional and new methods incl. (green) biotechnology

Structure of C18:4n-3 (Stearidonic acid)

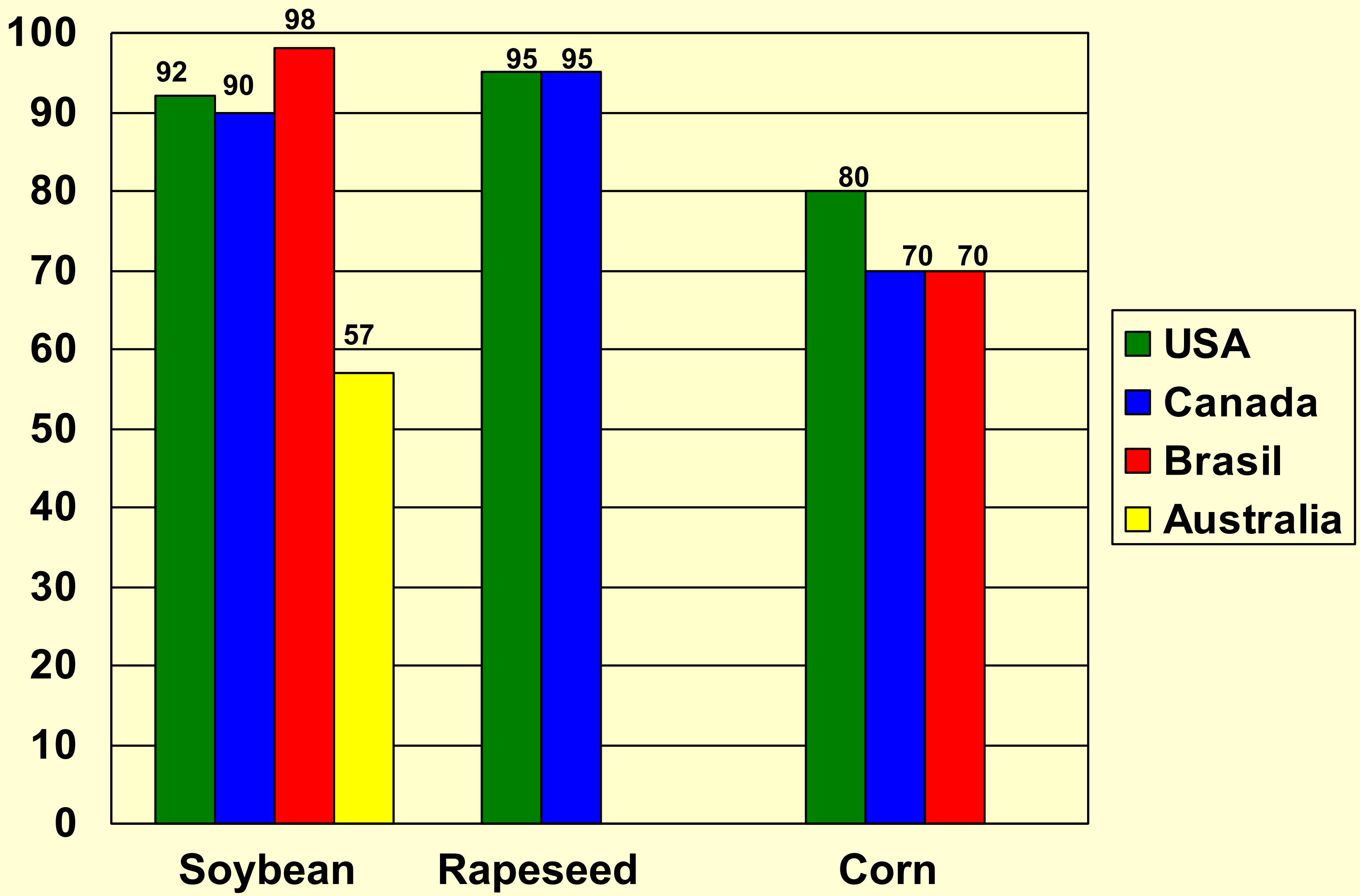


Stearidonic Acid (SDA) (18:4) 6c,9c,12c,15c

Events in commercial GM - crops and pipelines worldwide, by trait (Stein and Rodriguez-Cerzo, 2009)

Trait category	Commercial in 2008	Commercial pipeline	Regulatory pipeline	Advanced development	Total by 2015
Insect resistance	21	3	11	22	57
Herbicide tolerance	10	4	5	13	32
Crop composition	0	1	5	10	16
Virus resistance	5	0	2	3	10
Abiotic stress tolerance	0	0	0	5	5
Disease resistance	0	0	1	3	4
Nematode resistance	0	0	0	1	1
Fungus resistance	o	0	0	1	1
Other	2	0	0	11	13
Note: The number of trails can be bigger than the number of GM crops; Abiotic stress tolerance includes drough tolerance					

GM-area in various countries (% of total cultivated area, Toepfer Int. 2008)



Some recommendations from the „Best practices for the conduct of animals studies to evaluate crops genetically modified for input traits (GMP of the first generation)", adapted from ILSI (2003)

Animals (species/categories)	Number of animals (coefficient of variation 4 to 5 %)	Duration of experiments	Composition of dies [1]	Measurements
Poultry for meat production	10 to 12 pens per treatment with 9 to 12 birds per pen	5 weeks or more	Balanced diets	Feed intake, gain, feed conversion
Poultry for egg production	12 to 15 replications per treatment with 3 to 5 layers per pen	18 to 40 weeks of age, at least three 28-day phases	Balanced diets	Feed intake, egg production, feed conversion, egg quality
Swine	6 to 9 replications per treatment with 4 or more pigs per replication	Piglets (7 – 12 kg), 4 – 6 weeks Growers (15 – 25 kg) 6 – 8 weeks	Balanced diets	Feed intake, gain, feed conversion, carcass quality
Growing and finishing ruminants	6 to 10 replications per treatment with 6 or more cattle per replication	90 – 120 days	Balanced diets	Feed intake, gain, feed conversion, carcass data
Lactating dairy cows	12 – 16 cows per treatment 28 cows per treatment	Latin square: 28 day periods Randomized block design	Balanced diets	Feed intake, milk performances and composition, body weight, Body Condition Score (BCS), cell counts in milk, animal health

[1] Feed from GMP should be included in high portions in diets and compared with isogenic counterparts

Characterisation and steps for nutritional assessment of feeds from GM-Crops

Characterization of GMP	**GMP of first generation,** Plants with input traits, Feed without substantial changes in composition (Substantial equivalent)	**GMP of second generation,** Plants with output traits, Feed with substantial changes in composition
Steps for nutritional assessment	- Determination of major and minor nutrients and undesirable substances, - Principle of Substantial Equivalence (SE) - Case-by-case-studies to compare GM-feeds with isogenic counterparts in target animal species/categories	- Determination of major and minor nutrients and undesirable substances, -Determination of bio-availability/bio-potency of changed nutrients in target animal species/categories -Case-by-case (long-term) feeding studies to compare GM-feed with variously supplement isogenic counterparts in target animal species/categories