Slide 1

Genetic modification – Societal debate

Role of scientific knowledge

Clemens van de Wiel, Jan Schaart & Bert Lotz

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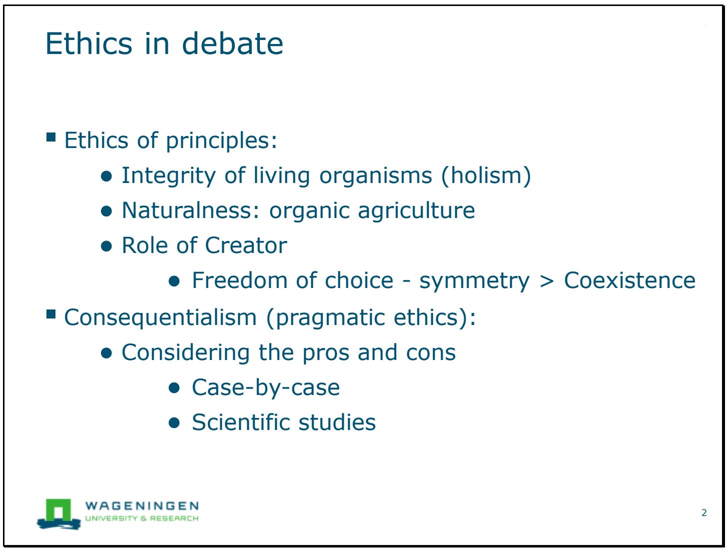
Slide 2



Ethics of principles related to convictions and beliefs. These are not suitable for a discussion involving scientific data, but call for an exchange of thoughts showing mutual respect and for enabling freedom of choice, enacted by coexistence rules. For recent review of organic principles and new breeding techniques, see e.g. Nuijten et al. (2017). In this ppt, pragmatic ethics are reflected in views widely held in society on sustainability (see the 3 themes People Planet Profit below), which may be subject to discussions in details (e.g. different views on socio-economic issues) and can be seen as "moving target": they develop with time based on experiences. However, GM crop performance can be assessed for PPP targets that have met with wide consensus in society, based on scientific studies.

Slide 3

Societal debate

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Credit: Virginia Tech Photo

Discussion during a visit of a field trial in the DuRPh programme for developing a cisgenic late blight-resistant potato (see slides below)

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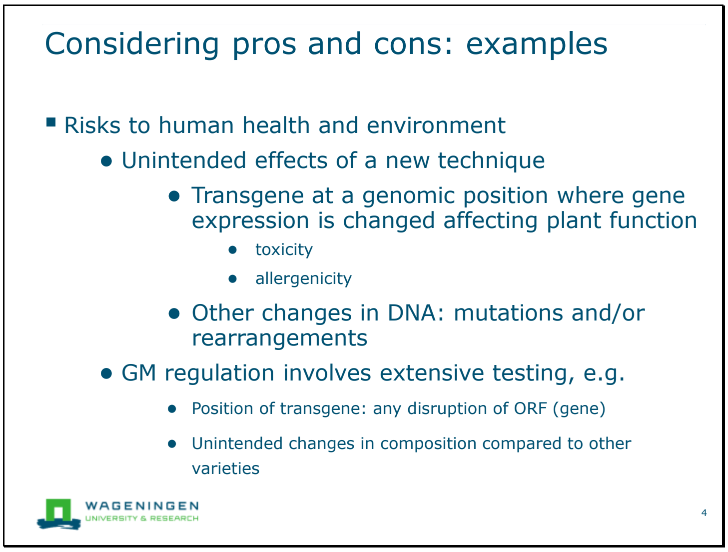

During breeding process, dysfunctional plants are removed from selections. In practice, no GM crops have been introduced that were found to be significantly changed in toxicity or allergenicity. Also, GM cultivars are much more similar to their direct comparator (parental plant line used in transformation) than cultivars to other cultivars, also when sharing similar pedigrees. ORF = open reading frame, indicating presence of a gene that may be disrupted in its function when a transgene would be inserted.

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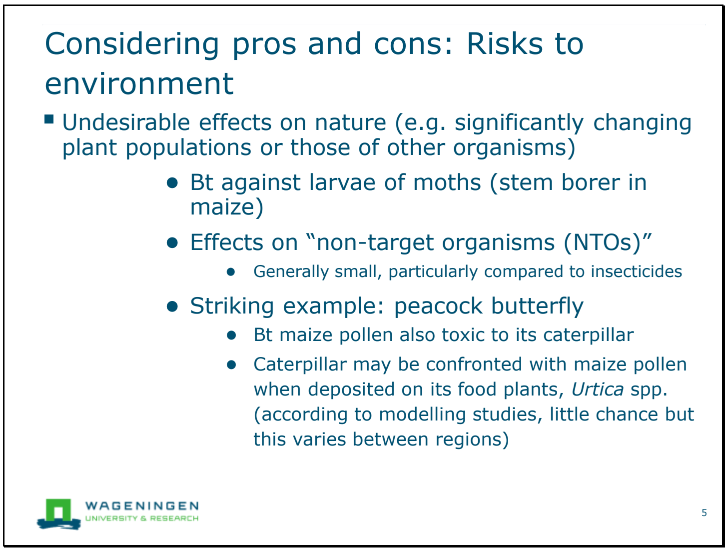

Bt = *Bacillus thuringiensis*, bacterial species that produces crystalline proteins (Cry proteins) that act as endotoxins (damaging to insect guts, Bt toxins or in brief, Bt), with different types specific to particular insect groups, e.g. Cry1Ab against lepidopterans (butterflies and moths) as in this slide, or Cry3Bb1 against coleopterans (beetles, e.g. rootworms). There are two aspects to potential negative NTO impacts. Organisms preying on or parasitizing the target pest (i.e. stem borer) that are important to Integrated Pest Management (IPM) may be harmed: this has been shown to happen, but usually as an indirect (and inevitable) consequence of the lower "food quality" of the pest as it has been damaged by the Bt and not by direct toxicity of Bt to the NTO (pest predator or parasite). The other is direct effects on NTOs occurring in maize fields: meta-analyses of studies have indicated that this is mostly not the case except sometimes for organisms related to the pest (e.g. other lepidopterans), these effects are usually small compared to those from chemical insecticides. These effects could be extended outside of the field, e.g. as in this example of the butterfly, due to Bt pollen dispersal. Chances of contact with Bt pollen may vary regionally: in N Europe only one generation per year, so lower likelihood of overlap with maize flowering period than in S Europe with two generations. EFSA has indicated chances overall are very low, based on modelling using toxicity levels and likelihood of exposure. For butterflies of conservation concern, EFSA recommends isolation distances of 20-30 m for maize cultivation to protected habitats (most maize pollen is shed close to fields, cf. isolation distances in coexistence, see ppt). This recommendation has been challenged in conservation literature, to which EFSA disagreed in an additional statement. A comparable discussion took place in the US on their local iconic species, the monarch butterfly. There was an additional possible factor there, i.e. that the use of HT crops, that is, the accompanying use of glyphosate, is bringing down the butterfly's food plant, milkweed (*Asclepias* spp.). No definite relationship was shown with monarch decline, but this is difficult to assess and continued monitoring would be useful (US NAS report 2016). It was one of the basically expected effects found in the large scale Farm-Scale Evaluations (FSE) in the UK around the turning of the century: the better the weed control (and this may be feasible with glyphosate, but also with other herbicides such as atrazine in the FSE, a herbicide that is not allowed anymore in the EU), the less weeds growing and thus also the less organisms (herbivores, pollinators etc.) depending on them, including their predators, parasites etc. (see further HT below). For another iconic insect, the honey bee, no significant effects of Bt were found and this species also is classified with another order of insects (Hymenoptera).

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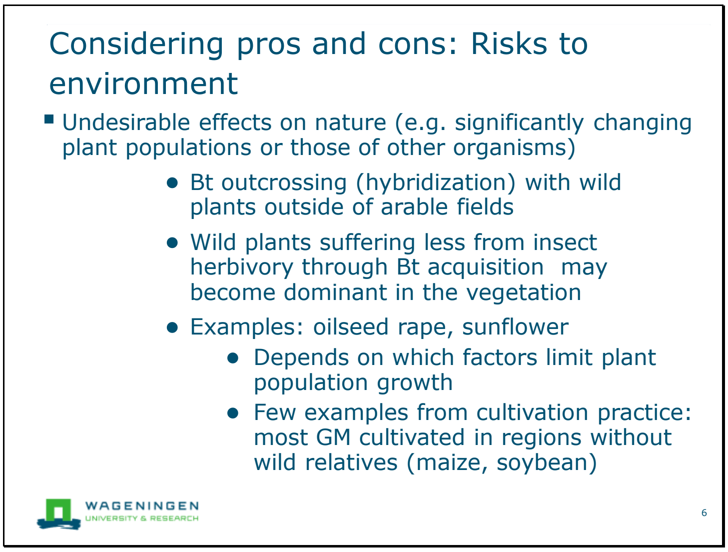

Fears with transgene “escape” to wild plant populations are that the Bt plants become predominant in large areas at the cost of genetic diversity in the wild species and/or that the wild species with Bt becomes “invasive”, that is, so abundant that other plant species are out-competed, with negative ecological consequences, also for other organisms. Persistence of transgenes in wild plant populations after hybridization to a GM crop is dependent on a large number of factors: genetic background, environmental conditions, stochastic factors (increase or decrease by chance, particularly in small populations). For instance, the position of the transgene in the genome: when linked to domestication genes conferring a disadvantage under natural conditions, chances of persistence will be lower, and the other way round with positively selected genes (e.g. tolerances to biotic or abiotic stresses). The presence of insects against which the Bt is effective is an important environmental factor. Furthermore, wild population growth will often be limited by other factors than herbivory by Bt-sensitive insects, e.g. other pathogens, competition with other plants etc. A disease that is problematic in cultivation, is not necessarily problematic in the wild, either because all individuals are already resistant to the pathogen or because other diseases are more prevalent etc. For Bt sunflower, it has been shown that under some field conditions the Bt plants were performing better than non-transgenic counterparts. However, the research was not continued so that it could not be determined whether the effect also applied in later generations, over the years. For that matter, GM work in sunflower almost completely stopped, because sunflower has wild relatives in the US and almost everywhere where it is cultivated, feral (“escaped”) sunflowers occur that could be subject to (trans)gene flow. Maize originates from Mexico, but GM maize is not cultivated there. There were several reports indicating that small admixtures occur in locally grown landraces. This may be due to mistakes, gene flow or introductions from imports. Smallholders sometimes use modern varieties to improve their own varieties (selections) and there is frequent exchange of seeds between farmers. Occurrence of GM maize is a sensitive issue because of the high cultural value of maize in local communities in Mexico (in which exchange of seeds is an important part). There is little known about whether GM maize has also dispersed to wild relatives (teosinte). For predictions of likelihood of gene flow, extensive modelling has been developed, but one has to take into account that there will likely remain a considerable margin of uncertainty (cf. De Jong & Rong 2013 Env Sci Pol 27:135) indicating need for prudency in environmental assessment requirements and more precision of what would count as transgenic harm in nature). Systems have been developed to limit gene flow, also with regard to coexistence, but these have been criticized as limiting the possibilities for growers to multiply the seeds themselves and for other breeders to use the seeds in their own programmes (discussions about so-called “seed terminator technology”).

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Considering pros and cons: Risks to environment

- Undesirable effects on nature (e.g. significantly changing plant populations or those of other organisms)
  - GM herbicide tolerance outcrossing of wild plants outside of arable fields
  - HT basically no advantage in nature, where no herbicides are sprayed
  - Example: oilseed rape
    - Ferals (“escapes”) along roadsides from seed spillage, populations do not show different growth from conventional oilseed rape
    - Possible problem in areas managed with herbicide (glyphosate on railroads)

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GM oilseed rape (*Brassica napus*) has been found to occur from seed spillage near harbours and other places where grain imports are transferred, also in countries without cultivation, e.g. Japan. In NL, oilseed rape is not very common (abundant “yellow crucifers” along roadsides are mostly other species), most populations from seed spillage are transient (but seeds may remain viable in soil for an extended period of time). For NL, with authorisation of imports, COGEM advised to monitor hotspots of seed transport (railroads). There is an additional possibility of hybridisation to other species, such as *B. rapa* that occurs as weedy species in NL. This has only been occasionally reported. It has also been reported for GM HT creeping bentgrass field trials in US (through gene flow to wild creeping bentgrass *Agrostis stolonifera* & ferals, extending further through hybridization with other grass species, *Polypogon monspeliensis*).
Occurrence of volunteers in arable fields and ferals outside may complicate coexistence (see coexistence ppt).

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Considering pros and cons: precautionary principle

- Risks to human health and environment
  - Precautionary principle: with uncertainty, progressing carefully, complex balancing of:
    - Which level of certainty is demanded for optimal regulation, as 100% safe is not achievable in scientific practice
    - With very strict safety rules, a novel plant variety could be withheld that could have offered large advantages, a chance missed on sustainability is also a loss to society ("innovation principle")

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Slide 9

Considering pros and cons: sustainability

- Sustainability, three themes:
  - "People": living and working conditions for people
  - "Planet": decreasing environmental impact
  - "Profit": commercial viability and revenues for growers, processors and consumers

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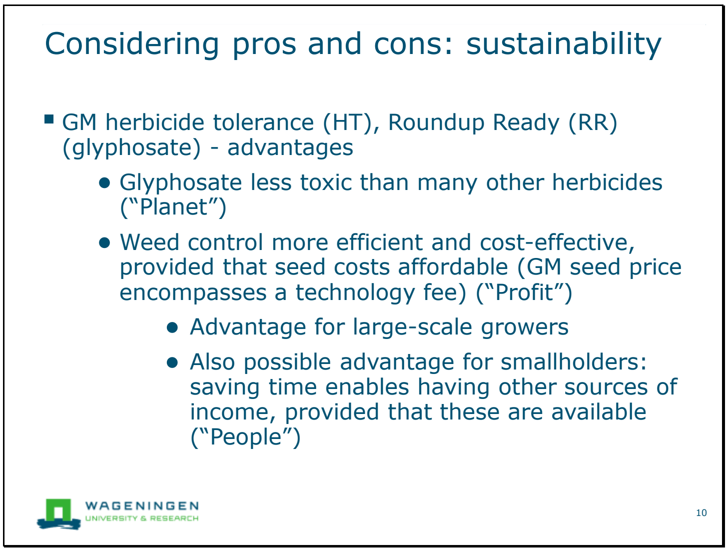

Toxicity of glyphosate controversial in the media (as is the combination with RR crops, both developed by Monsanto): much attention from NGOs and discussions about scientific studies.
By IARC (WHO) characterized as potentially carcinogenic, but according to Echa (European Chemicals Agency) not classifiable as carcinogenic
By European agency EFSA recently characterized as safe to use in an agricultural context
IARC = International Agency for Research on Cancer (WHO = World Health Organization). EFSA = European Food Safety Authority.

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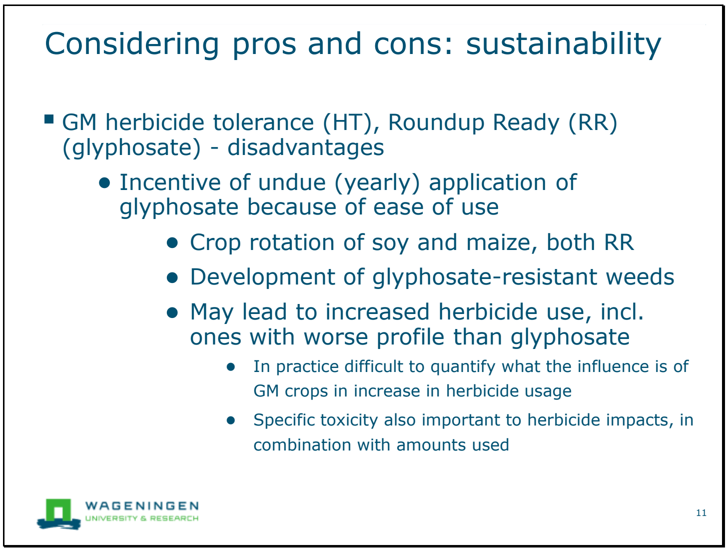

Increase in herbicide use complex issue: some studies point to a relationship between herbicide-resistant weeds and an increase in herbicide use, at least the expected decrease shortly after GM introduction soon disappeared. This is not always clear and moreover, toxicity level of glyphosate also important: being lower than other commonly used herbicides, impact may still be lower even when use in terms of amounts (kg) is higher. There are far less studies well addressing herbicide impacts. In addition, at the same time, herbicide usage has also increased in conventional crops in US. There are also weeds resistant to other herbicides than glyphosate, presently used in GM.

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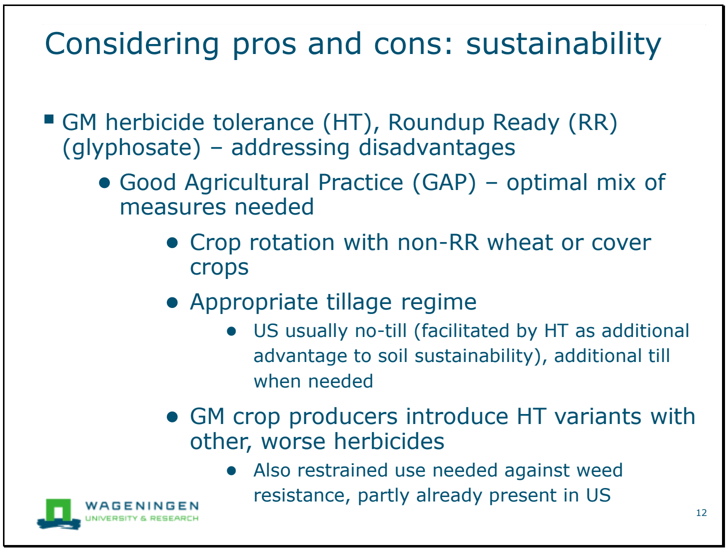

There is no GM HT wheat on the market (was developed, but never implemented up to now).
HT logical advantage for “zero-till”: sowing can be easily performed after only a herbicide treatment. Zero-till not completely dependent on HT, also implemented without HT. Organic matter sequestration also dependent on other factors, such as treatments at other times in rotation. Also disadvantages to zero till, such as increased disease pressure.
Resistances against some of the alternative herbicides already present in EU as well.

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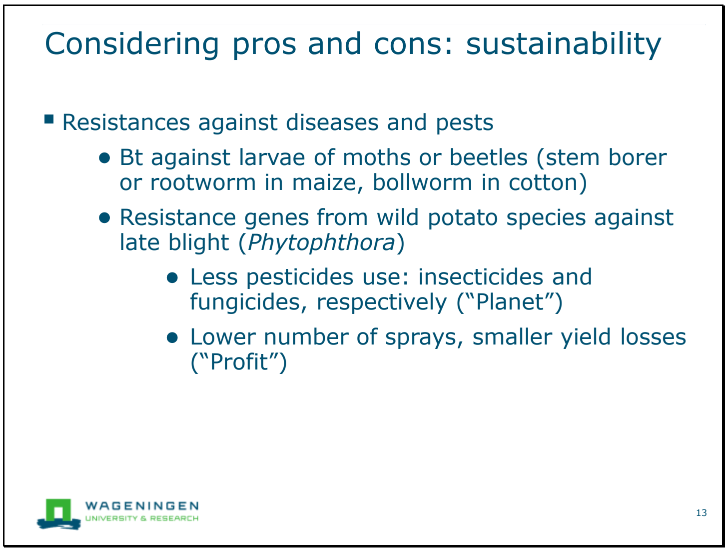

Bt may even be used as sprays in organic cultivation (as last resort). Bt in eggplant (brinjal in India) against fruit and shoot borer, developed in India, yet presently strong opposition against GM in India. Therefore as of yet only extensive Bt cotton cultivation in India (already introduced early 2000s). Bt brinjal cultivation only started in Bangladesh.
Difficult to target corn borer inside maize plants (stems) by insecticide sprays, so conventional farmers will not always apply insecticides; against rootworm, insecticides in seed coatings can be used.
Indications for general decrease of pest insect populations by large-scale use of Bt crops; thus, also non-Bt growers may enjoy some protection against herbivory.
Many studies on Bt cotton in China and India, generally indicating better yields and labour safety due to reduced insecticide use. However, also lots of variation between farmers: cotton is risky cultivation for small farmer, potentially high revenues but also high investments with risks of debt when harvest fails, harvest not only dependent on Bt but also availability of water and fertilizer, reliable cultivar seed lots and accompanying cultivation knowledge etc, which were not always well supported, particularly at the beginning of Bt cotton cultivation in India. In the beginning, Bt was not yet available in varieties adapted to each local growing condition in India. Later on, more varieties became available and also more Bt variants, e.g. developed in China. Also, "pirate" Bt seed was circulating in the beginning of Bt adoption, which could make seeds more easily and cheaply available to growers (and provide an opportunity to experiment with the crop) but also lead to all sorts of seed quality problems. In the end, profitability of Bt depends on risk of infestation weighed against higher seed costs and the importance attached to harvest security provided by Bt.

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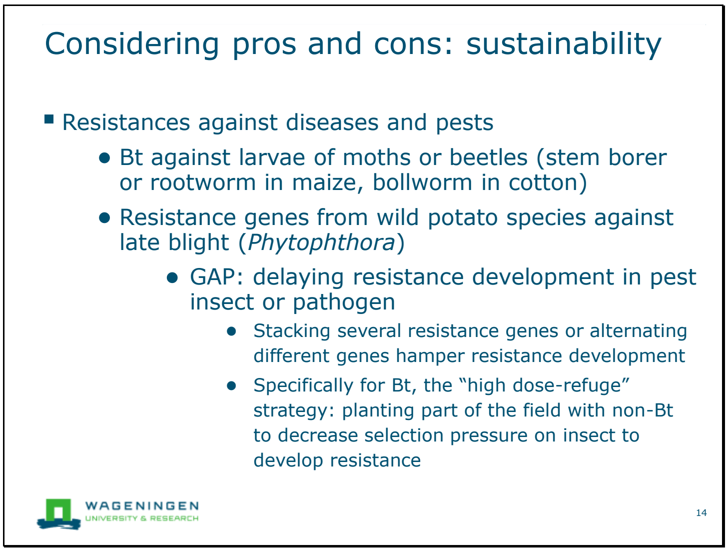

Bt resistance management by so-called "high dose – refuge" strategy: production of sufficient amounts of strongly insect-impacting Bt in the plant so that also insects heterozygous for Bt resistance are killed, at the same time maintaining influx of alleles for sensitivity to Bt in the refuge consisting of non-Bt plants. With low insecticide use consequent to Bt cultivation, additional risk of the rise of secondary pests, i.e. insects sensitive to insecticides but insensitive to Bt (e.g. aphids or other sucking insects), thus there may be a need for monitoring the crop for this.
There are recent examples of resistance development in pest insects, partly by poor management and/or too low effective levels of Bt in plant (e.g. with maize rootworm).

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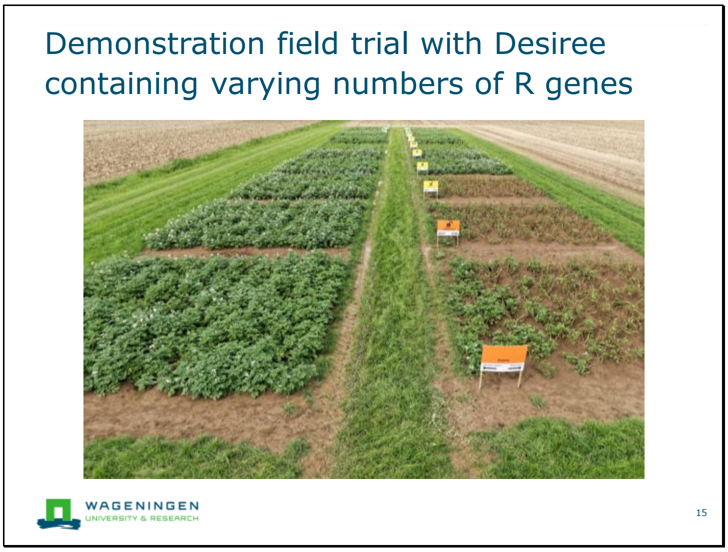

From front to back: Desiree, Desiree with 1 R gene, 2 R genes, 3 R genes. Left: support of resistance by fungicide spray; right: no spray.

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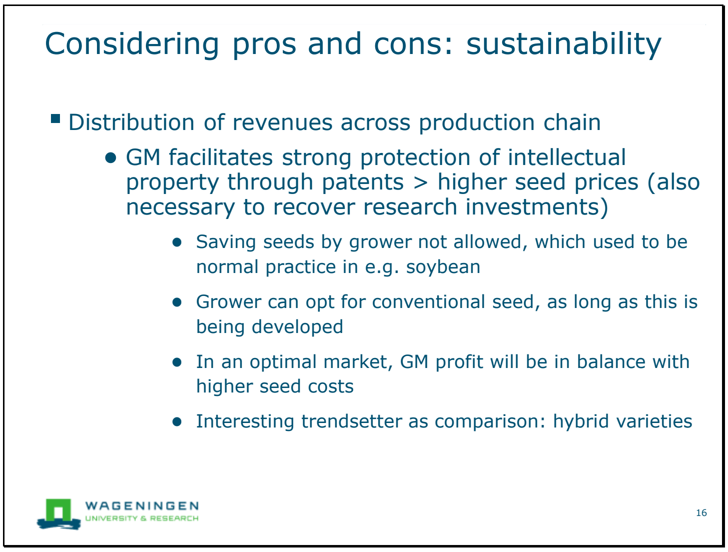

For details on hybrid varieties, see Hybrid cultivars ppt, where developments in maize since last century are mentioned: development of hybrid maize led to significant increases in yield and to a shift of seed saving (selections) by farmers to seed production by breeders. This made maize a more profitable crop for breeding than wheat, for which still seed saving can be a normal practice (and hybrid breeding is actively researched). GM wheat has been developed, but not introduced, which will be related to possible market problems outside of US. Like wheat, soybean as selfing crop was attractive for seed saving practices, which have largely decreased with the high adoption of GM soybean. Conventional soy breeding still practiced at universities in US, which does not have the levels of investments as large breeding companies. In EU, growers are often more used to buying certified seed lots each year. With regard to optimal markets, Bt maize prices in Spain appeared to have a relationship with infestation levels (Gómez-Barbero et al. 2008).

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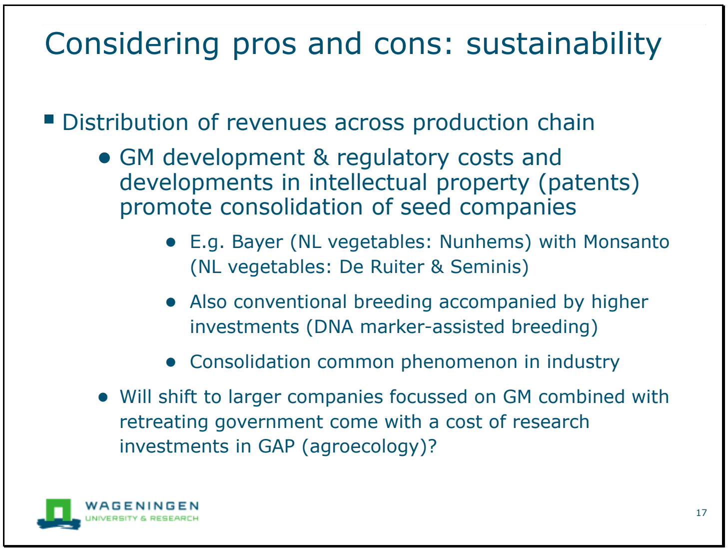

Producing a dossier for the safety assessments by regulatory authorities is a costly affair. This is regarded as prohibitive to GM applications by small breeders and for small crops.

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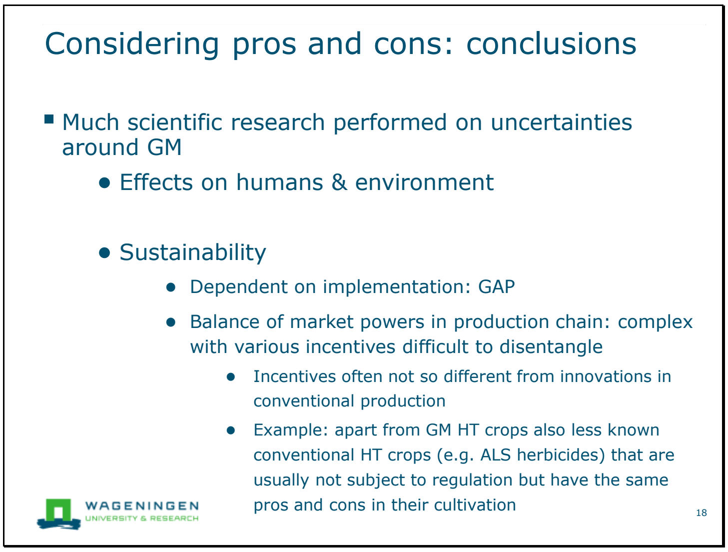

ALS = acetolactate synthase (also called AHAS = acetohydroxy acid synthase), enzyme involved in biosynthesis of branched-chain amino acids, ALS herbicides inhibit the working of this enzyme. HT crops for ALS herbicides can be produced by classical mutagenesis (or selecting spontaneous mutations) of ALS enzyme gene: e.g. “Clearfield” IMI oilseed rape and sunflower (uniquely regulated as novel trait under the Canadian system), presently also such a sugar beet in pipeline in Europe (Conviso-Smart). Weed control is relatively difficult in sugar beet, introduction of GM RR sugar beet was an immediate success in the US. Growers in the EU could also be interested in RR sugar beet. Its advantage would however be diminished when weed beets would obtain the HT for glyphosate by hybridization with bolters in the RR sugar beet.