OBJECTION TO BAYER CROP SCIENCE'S APPLICATION FOR COMMODITY CLEARANCE OF GENETICALLY MODIFIED COTTON LL 25

AFRICAN CENTRE FOR BIOSAFETY
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1 INTRODUCTION

Bayer CropScience has submitted an application to the Executive Council established under the Genetically Modified Organisms Act in South Africa, for commodity clearance of its Liberty Link 25 (LL25) genetically modified (GM) cotton. This is the first ever application for commodity clearance to enable the importation of GM cotton into South Africa.

To date, Australia and the United States have approved LL25 for commercial growing while Canada, Japan, Korea and Mexico have approved it for importation as food and feed Clearly Bayer's application to the South African authorities is part of its global strategy to penetrate the GM cotton market. If the Executive Council grants the application, it will open the doors for the importation into South Africa of GM cotton from the US, where cotton production is heavily subsidized. It is well documented that these subsidies are destroying livelihoods in Africa and other developing regions.

South Africa's cotton production is small, averaging around 20 000 ha for 2006/7 and steadily declining. Although 90% of South Africa's own cotton production consists of GM varieties, this production contributes minimally to South Africa's overall consumption. Indeed, South Africa imports cotton from several countries in the Southern African Development Community (SADC), especially Zimbabwe, Zambia, Mozambique and Botswana. Bayer's application if granted, will severely impact on and have far-reaching ramifications for the livelihood of cotton farmers and rural populations who rely on cotton as a cash crop and farm income, quite apart from the loss of revenue for SADC governments and the concomitant negative socio-economic consequences flowing from this.

2 SUMMARY OF SCIENTIFIC ASSESSMENT

1. We have found that the results of the Southern blots to be unclear and lacking the sensitivity to detect all the expected fragments. More importantly, the data furnished by Bayer only looks at individual plants and does not use several plants for the study;
2. The use of the *CaMV* promoter generates a recombination hotspot, which causes increased rearrangements and gene instability. This transgenic instability raises many known and unknown risks including altering plant gene expression and metabolism, and the possible generation of new viruses;
3. The direct effects on human health and any adverse effects are related to the consumption of the processed seed (oil) or cotton linter fiber and cotton cake is used as a feed for livestock. Of main concern is the higher levels of free Gossypol in *Gossypium barbadense*.
4. In the USA the maximum recommended amounts of gossypol in cattle feed is 0.05-0.01% free Gossypol (Kirk and Higginbotham 1999). The LL25 contains levels of approximately 0.5% fresh weight BK02B005.PG 22 TABLE8). If the cake is used in an amount more than 10% of the animals feed, health problems can be expected, including male sterility;
5. Of additional concern is that the company data show that LL25 cotton- seed contains significantly less vitamin E than the non-transgenic cotton (83.6 IU/kg compared to 187.8 IU/kg - table 7, BK02B005). It is therefore a poorer quality feed;
6. About 40-60% of cottonseed passes through the animal gut and into the environment. Soil bacteria will be exposed to the transgenic DNA where is may be taken up and incorporated into its genomic DNA (horizontal gene transfer, HGT);

7. Resistance to phosphinotricin has been found in bacteria from five other genera. HGT to soil bacteria from plant leaf material has been shown to occur. The fact that bacteria contain DNA sequences similar to the bar gene (transacetylases) will increase the likelihood of homologous recombination and HGT. The release of transgenics containing antibiotic resistance genes will spread antibiotic resistance genes to pathogenic bacteria in the soil thereby compromising the ability to treat current and future diseases.

3 PROFILE OF BAYER

3.1 BAYER CROPSCIENCE

Bayer is a Germany-based transnational corporation with 350 offices on five continents. It is best known worldwide for its aspirin. The cornerstones to the company are in Europe, North America and the Far East with a growing presence in China. Bayer **AG**, the main Bayer corporate name, is now a management holding company with several subsidiaries. Bayer AG is a massive Germany based chemicals and pharmaceuticals manufacturer, and it is a key player in the development, commercialization and sale of GM crops.

The Bayer subsidiary dealing with crops is Bayer CropScience AG. Bayer Cropscience was founded in 2002 after buying out Aventis Cropscience, which is known for its contamination scandal in the UK, which involved 'Starlink' maize. The company's Crop Protection unit makes fungicides, herbicides, and insecticides. Bayer CropScience also has two other divisions, Environmental Science and BioScience, that focus on non-crop chemicals (such as consumer lawn care products) and genetically engineered seeds, respectively.

3.2 Bayer In South Africa

Bayer Cropscience has been forced out of the UK, withdrew its plans to commercialise GM canola in Australia, and have abandoned its research in India. Bayer Cropscience, has dumped toxic waste in the South Durban Basin, which led to water being contaminated with chrome VI, a carcinogenic toxic substance. Bayer has bankrolled GM sugarcane research in the hope that it could corner the GM sugar to ethanol biofuels market and has also applied to the South African authorities for a commodity clearance of its risky GM rice, LL62.

3.3 Bayer and GM Rice contamination

2006 will go down in history as the year Bayer's Liberty Link (LL rice 601) unapproved GM rice contaminated commercial trade around the world and food aid in Africa (Sierra Leone and Ghana).

4 SOCIO-ECONOMIC REVIEW

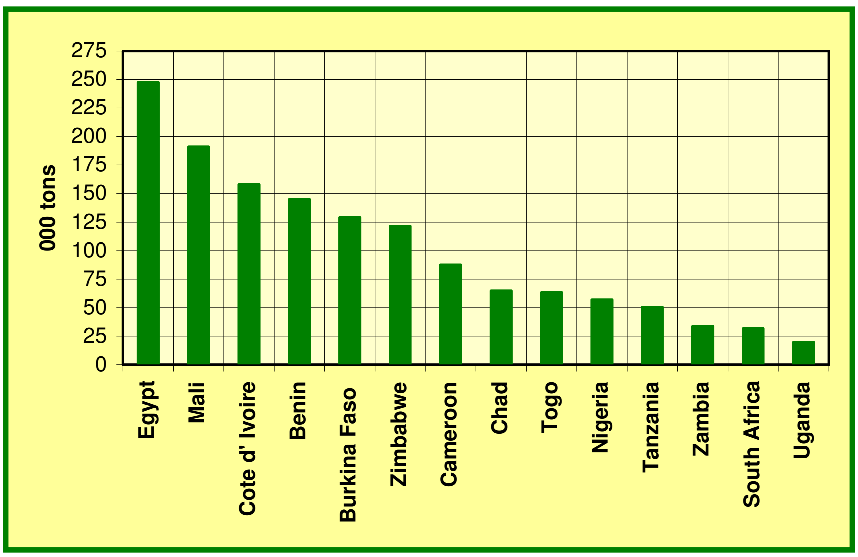
4.1 Cotton Production In Africa

(Sections 4.1 and 4.2 has been taken from research conducted for the African Centre for Biosafety by Stephen Greenberg)

Cotton and handicraft cotton textile production were part of African economies, in particular in West Africa, long before the arrival of colonists. Cotton production for export took off from the early 1960s in West Africa. Production of seed cotton rose from 30 000 tons in 1960 to 1.9m tons in 2002 with 95 per cent of lint produced in the region being exported. Sub-Saharan Africa as a whole recorded a 175 per cent increase in cotton production between 1993 and 1998.

A fairly broad estimate is that in 2002 Africa contributed around 8-10 per cent of global production and around 15-18 per cent of global exports. Thirty African countries produce cotton, the most significant being Egypt in North Africa, and Mali, Cote d' Ivoire, Benin and Burkina Faso in West Africa.

Figure 1: Cotton production in selected African countries (5 year average, 1998/99- 2002/03)

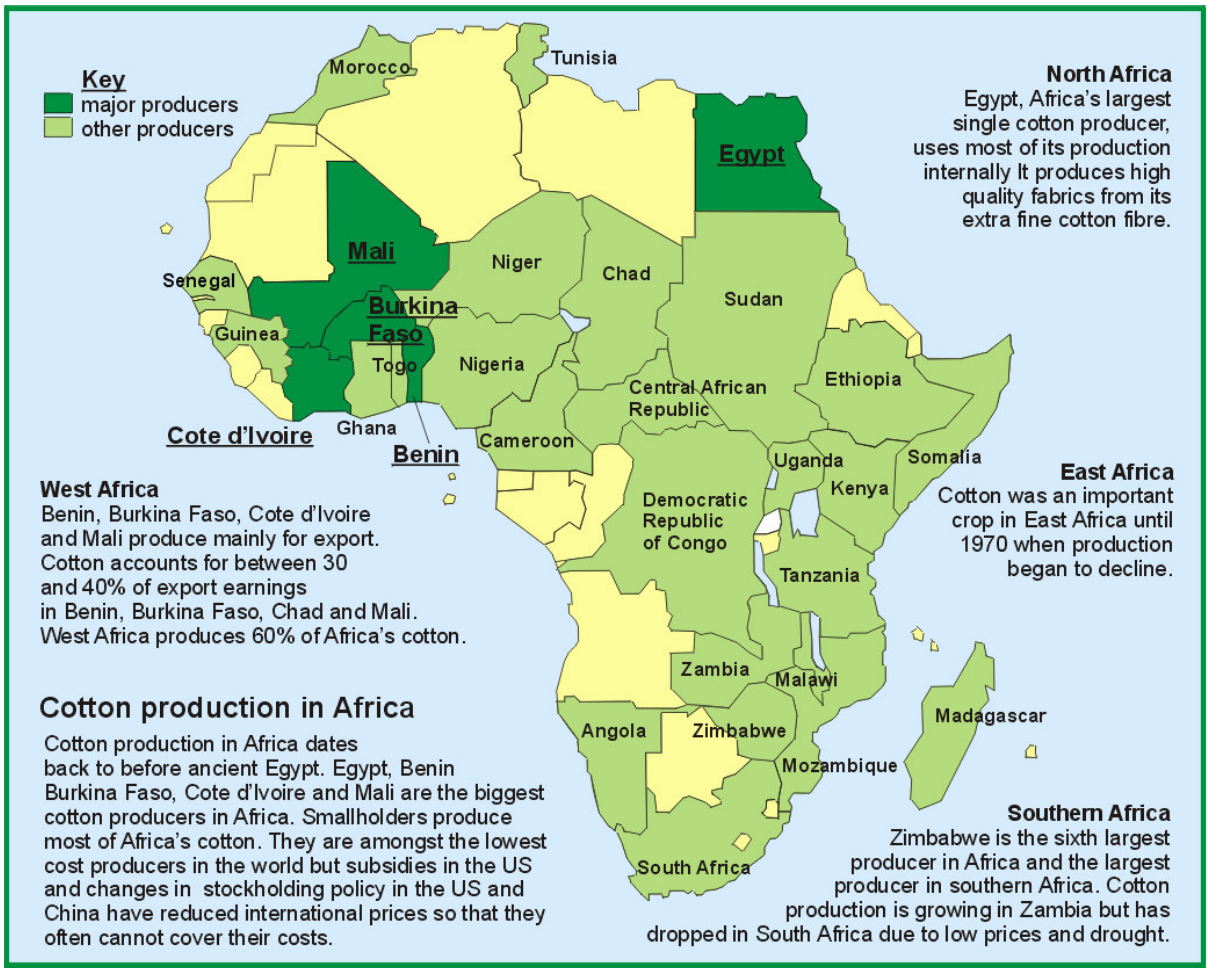


Source: Data from Baffes 2004:59, 71, 72

Between them, these five countries produce slightly less than two-thirds of Africa's total production. Egypt uses most of its own production domestically, while the West African countries produce mainly for export. In the 1980s, cotton exports from Africa rose dramatically, although from a low base. The overwhelming majority of African cotton is exported as lint, that is after the first step of separating seed and fibre.

Cotton exports are very important for the economy of West Africa accounting for approximately 40 per cent of all merchandise export earnings in Benin and Burkina Faso, and 30 per cent in Chad and Mali. On estimate more than 10 million livelihoods depend on the cotton industry in West and central Africa, with cotton a typical, and often dominant, smallholder cash crop. Although they are amongst the cheapest cotton producers in the world subsidies have skewed the market to the extent that West and central African producers receive only 60 per cent of their costs and prices have dropped 31 per cent despite a 14 per cent increase in yields in recent times.

4.2 Map Of Cotton Production In Africa



Egypt in North Africa is the largest single cotton producer on the continent. However, domestic consumption accounts for more than half its production and the country does not export much raw cotton. Egypt has a strong spinning and weaving industry, and produces high quality fabrics from long staple extra fine cotton fibre. Other North African countries producing cotton are Morocco and Tunisia.

In East Africa cotton was an important crop before the 1970s. However, since then cotton's share of production has declined. Uganda, Ethiopia, Kenya, Somalia and Sudan all produce some cotton. Since liberalisation, cotton production in the region has shifted to a low-input basis and export strategies target the 'market window' when there is a limited supply of new cotton coming onto the market from other parts of the world.

Zimbabwe and, following some way behind, Tanzania are the largest cotton producers in Southern Africa. Zimbabwe is the sixth largest cotton producer in Africa exporting a significant share of the crop. Cotton production in Zambia has grown quite significantly since 1995, while South Africa's cotton production has dropped since the mid-1990s and particularly in the new millennium following low prices and drought. Mozambique, Angola and Malawi also produce small amounts of cotton.

4.3 South Africa's cotton trade with Africa

In South Africa, local cotton production is protected in that cotton mills are compelled to buy South African fibre first and can only import cotton once local supplies have been exhausted. However, currently South African cotton production is at an all time low due to low global cotton prices. As a result, South Africa imports between 80 and 90% of its cotton consumption from its neighbours in the sub-region, the Southern African Development Community (SADC), especially from Zimbabwe, Zambia and Mozambique. According to free trade agreement between SADC countries (in force since 2000 called the Southern African Customs Union Agreement 'SACU') there has been no duty on cotton imports from these countries since

1st January 2004. Other countries in SADC exporting cotton to SA include Botswana, Namibia and Mozambique, where whole cotton- seeds are imported into South Africa where the ginning also takes places.

According to the National Department of Agriculture's website, during the 2003/4 marketing season, 84 % of South Africa's cotton lint needs came from SADC with Zimbabwe and Zambia contributing 30% and 39% respectively. Non-SADC countries contribute 16% of South Africa's cotton needs with the US only accounting for 1% of lint imports. The table below is instructive of South Africa's trade with Zambia and Zimbabwe as well as other countries in SADC, for the last ten years.

COTTON LINT PRODUCTION, IMPORTS, CONSUMPTION & EXPORTS

(Swaziland included) **TON**

MARKETING YEAR	PRODUCTION*	LINT IMPORTS FROM: ZIMBABWE	ZAMBIA	OTHER	TOTAL LINT CONSUMED	EXPORTS	AVG. RSA LINT PRICES*** (RSA c/kg)
1997/98	31 134	24 187	#	27 661	83 610	0	795
1998/99	42 381	17 143	3 121	17 736	69 463	11 113	810
1999/00	53 144	11 322	9 310	8 553	75 058	6 139	820
2000/01	29 768	18 852	6 939	3 931	65 115	1 256	764
2001/02	38 634	18 516	9 211	9 901	72 826	0	962
2002/03	21 228	16 864	23 096	11 632	77 427	0	1179
2003/04	16 348	14 150	18 218	14 255	61 929	0	1102
2004/05	28 021	9 651	12 607	7 179	59 224	0	1109
2005/06	22 041	1 660	18 174	7 576	48 186	6 599	737
2006/07**	14 896	11 840	17 995	9 277	46 515	7 733	850
2007/08***	12 287	est. 40 000 total imports			47 000	5 000	

* *Lint produced in the RSA & Swaziland from RSA, Swaziland, Zimbabwe, Mozambique and Botswana seed cotton.*
** *Preliminary* *** *Estimates* *# Zambia included in other*

Source: Cotton SA www.cottonsa.org.za

4.4 Killing the SADC cotton market: US subsidized cotton

The subsidization of US cotton has been thoroughly documented, and its concomitant effect on global cotton prices and cotton growing countries in Sub-Saharan Africa. The scale of the US government support to its 25,000 cotton farmers is staggering. According to Oxfam, every acre of cotton farmland in the US attracts a subsidy of $230, or around five times the transfer for cereals. In 2001/02 farmers reaped a bumper harvest of subsidies amounting to $3.9bn – double the level in 1992. To put this figure in perspective, America's cotton farmers receive:

- more in subsidies than the entire GDP of Burkina Faso – a country in which more than two million people depend on cotton production. Over half of these farmers live below the poverty line. Poverty levels among recipients of cotton subsidies in the US are zero.
- three times more in subsidies than the entire USAID budget for Africa's 500 million people.

Using data from an International Cotton Advisory Committee model, Oxfam has attempted to capture the cost to Africa of American cotton subsidies in 2001/02. For the region as a whole, the losses amounted to $301m. Eight cotton-producing countries in West Africa accounted for approximately two-thirds ($191m) of overall losses.

The small size of the countries concerned and their high level of dependence on cotton magnify the effect of US policies. For individual countries, US cotton subsidies led to economic shocks of the following magnitude:

- Burkina Faso lost 1 per cent of GDP and 12 per cent of export earnings.
- Mali lost 1.7 per cent of GDP and 8 per cent of export earnings.
- Benin lost 1.4 per cent of GDP and 9 per cent of export earnings.

5 SCIENTIFIC SAFETY ASSESSMENT

In response to the African Centre for Biosafety's (ACB) application for access to information to Bayer's application and risk assessment data, the ACB was furnished with more than 1500 pages of data. We have thoroughly canvassed this data and present our safety assessment findings as set out below.

5.1 The Transgenic construct

LL25 was constructed first by creating a transgenic *Gossypium hirsutum* cotton containing the *bar* gene under the control of the cauliflower mosaic promoter, *CaMv*. The transgenic *Gossypium hirsutum* cotton was crossed with the closely related species, *Gossypium barbadense* to produce LL25. LL25 therefore contains the antibiotic résistance gene, *bar*, from the bacteria *Streptomyces hygroscopius* that confers resistance to phosphinotricin, an herbicide. It also contains genetic characteristics inherited from the cross with *Gossypium barbadense*- an extra long staple fibre that makes it preferable for high quality cotton fibre.

5.2 Genetic Stability

To determine what genetic changes were introduced into LL25, data is presented on the copy number and site of insertion of the transgenic cassette into the cotton genomic DNA. However, we have found that the results of the Southern blots to be unclear and lacking the sensitivity to detect all the expected fragments (Appendix 11, pg18 fig 6 and 7 of application). More importantly, the data furnished by Bayer only looks at individual plants and does not use several plants for the study.

Is the insertion point the same for several (>20) plants grown in the field? This important question addresses genetic stability. From other evidence it would appear that use of the *CaMV* promoter generates a recombination hotspot to cause increased rearrangements and gene instability (Kohli *et al* 1999). PCR of genomic DNA from several plants (population of 20+ individual plants) with primers flanking the genetic elements of the transgenic cassette and DNA sequencing of selected PCR products should be carried out. Experiments using comparative genomics are required to fully establish genome stability of transgenic lines.

Techniques such as repPCR, RAPD and comparative genome hybridization (CGH) have been shown to be effective in establishing genome similarity (Bao *et al.* 1993, Pinkel and Albertson 2005). This is required since fragmenting and scattering of the transgenic cassette in the genome (transpositions with rearrangements and deletions) may result in loss of the primer binding sites or a large distance (>10kBp) between genetic elements of the cassette, giving in false negative results by when detection is carried out by standard PCR.

It is therefore not certain if there are rearrangements of the transgenic cassettes and genetic instability. There are, however, known problems with the genetic instability of transgenic constructs containing the *CaMv* viral promoter (Kohli *et al* 1999). This transgenic instability raises many known and unknown risks including altering plant gene expression and metabolism, and the possible generation of new viruses.

5.3 Effects On Human And Animal Health

In South Africa, approximately 30% of the imported cotton is as a fibre 30% as seed and 30% as seed cake. A small proportion <0.3% of cotton linter fiber is used as a thickener in baked goods, dressings, snacks. Therefore the direct effects on human health and any adverse effects are related to the consumption of the processed seed (oil) or cotton linter fiber. The cotton cake is used as a feed for livestock (cattle, poultry, swine, catfish) (OGTR 2002).

Of main concern are the higher levels of free Gossypol in *Gossypium barbadense* (Pima varieties) (Sullivan *et al.* 1993). The toxicity of gossypol is well documented causing heart and liver damage (Lindler 1990) with poisoned cattle displaying symptoms of difficulty in breathing, weakness, diarrhea and death (Kirk and Higginbotham 1999). In the USA the maximum recommended amounts of gossypol in cattle feed is 0.05-0.01% free Gossypol (Kirk and Higginbotham 1999). The LL25 contains levels of approximately 0.5% fresh weight BK02B005.PG 22 TABLE 8). If the cake is used in an amount more than 10% of the animals feed, health problems can be expected. Gossypol also causes male sterility (Brocas et al).

There is surely no mechanism whereby this information has been passed on to the farmer to prevent animal toxicity. This is particularly true if farmers are used to supplies of seed cake from low or Gossypol free varieties such as *Gossypium hirsutum*. Of additional concern is that the company data show that LL25 cotton seed contained significantly less vitamin E than the non-transgenic cotton (83.6 IU/kg compared to 187.8 IU/kg - table 7, BK02B005). It is therefore a poorer quality feed.

A study on chickens compared LL25 treated with herbicide, LL25 not treated with herbicide and the parental non-GMO cotton not treated with herbicide (Appendix 16, Study #13798.4100). The authors incorrectly concluded that there was no effect of GM cotton on the health (weight gain) of developing chicks. While there was no difference between chicks fed LL25 treated with herbicide and the parental non-GMO cotton not treated with herbicide there was a significant difference between LL25 not treated with herbicide and the parental non-GMO cotton not treated with herbicide. The authors report this "a significant difference between Group A (commercial variety) and Group C (LL25, not treated with herbicide)…the mean breast weight for these two groups were 169.4g and 154.1g respectively". However, they dismiss this finding since they cannot explain it. (pg28 of Appendix 16, Study #13798.4100). This misinterpretation is highly relevant since it suggests that LL25 cotttonseed meal may be an inferior livestock feed.

5.4 Environmental effects

5.4.1 HGT to soil microbiota: effects on soil health

The digestibility of whole seeds by animals such as cattle is only 5%. Therefore, the cotton-seed is usually cracked and this results in a digestibility of 40-60% (Sullivan *et al* 1993). This means that 40-60% passes through the animal gut and into the environment. The effects on soil the biodiversity and functioning of soil microbiota has not been considered. Soil bacteria will be exposed to the transgenic DNA where is may be taken up and incorporated into its genomic DNA (horizontal gene transfer, HGT).

Phosphinotricin originates from the bacteria *Streptomyces viridochromogenes Streptomyces* hygroscopicus and several other *Streptomyces* species. It acts as an inhibitor of glutamine synthetase and therefore has herbicide and antibiotic activities- it is active against Gram-positive and Gram-negative bacteria as well as against the fungus *Botrytis cinerea* (Bayer *et al.*, Helv. Chim. Acta 55 (1972) 224).

Resistance to phosphinotricin has been found in bacteria from five other genera (Bartsch 1989), suggesting that they contain homologs to the bar/PAT gene. HGT to soil bacteria from plant leaf material has been shown to occur (despite the large excess of plant DNA) and is most efficient where sequence homology is present (de Vries and Wackernagel 1998). The fact that bacteria contain DNA sequences similar to the bar gene (transacetylases) will increase the likelihood of homologous recombination and HGT

Furthermore, the probability HGT is increases because this genetic construct LL25 contains the *CaMV* promoter.

The biosafety risks of the viral *CaMV* promoter include increased recombination (rearrangements, deletions, insertions). There is evidence from the laboratory (Kohli *et al.* 1999) and field studies (Quist and Chapela 2001, Collonier *et al.*, Ho *et al.* 2000) that the *CaMV* is a recombination 'hotspot'. The *CaMV* results in very high expression levels that may result in unintended (pleiotropic) effects from the expressed transgenes. Increased recombination with other viral elements and the creation of new viruses (Wintermantel *et al.* 1996, Vaden and Melcher 1990, Greene *et al.* 1994).

This new genetic material acquired by HGT will only be retained if it has a selective advantage. The regular application of phosphinotricin herbicides will ensure a selective advantage.

There may also be advantages in the absence of applied herbicide. Many antibiotics are produced by Actinomycete bacteria to kill competing bacteria in the soil; therefore acquiring phosphinotricin antibiotic resistance may acquire a selective advantage *per se*. Selective pressures may also include several stresses such as soil tilling or application of agrochemicals since current evidence suggests that a stress response facilitates the HGT and spread of antibiotic resistance genes. For example the SOS response—induction of specific genes in response to DNA damage—alleviates the repression of genes necessary for the horizontal gene transfer of the mobile genetic element conferring resistance to the antibiotics chloramphenicol, trimethoprim, streptomycin, and methoxazole. (Beaber *et al*., 2003).

Mobile genetic elements have played a key role in spreading antibiotic resistant genes amongst bacterial populations and contribute to multiple antibiotic resistance of bacterial pathogens (Nikolich, *et al.* 1994; and Witte, 1997). Therefore, there are risks associated with the spread of antibiotic resistance genes amongst soil bacteria, even when there is no selection for the transgenic construct *per se*. The effects from these changes in soil biodiversity and soil ecosystem functioning have not been considered.

The release of transgenics containing antibiotic resistance genes will spread antibiotic resistance genes to pathogenic bacteria in the soil thereby compromising the ability to treat current and future diseases. Even though phosphinotricin–based antibiotics are not currently being used to treat human diseases, they represent an arsenal for development of new antibiotics. Health experts worldwide are concerned about the spread of antibiotic-resistant microbial infections and the shrinking arsenal of compounds that can effectively treat them (see MRSA/drug resistance news 29 April 2007).

5.4.2 Weediness and Hybridization

As mentioned, approx 30% of imported cotton is seed (in 2004 114 490 tonnes of cottonseed imported, Table1). The dossier states that it is "not expected that cottonseed, once imported into South Africa, will be transported to cotton growing areas". However, experience over the last 10 years with transgenic crops indicates that containment in the wider environment is very difficult. This can be due to human error or illegal seed sales and planting. For example, transgenic DNA found in traditional maize landraces in Oaxaca, Mexico (Quist D and Chapela IH. Nature 2001, CONABIO) confirmed these findings- *Science* 1 March 2002). This contamination of landraces occurred despite GM maize never being approved in Mexico.

Certified non-GM canola seedlots grown in western Canada contained transgenic herbicide-tolerance traits after only 6–7 years of commercial production of GM canola in Canada. Between 59%-97% of the seedlots contained more than 0.01% transgenic DNA. This level of contamination in pedigreed seed is noteworthy and disturbing because it shows that even stringent segregation systems were not sufficient to deliver pure non-GM canola seed to farmers in western Canada (Friesen *et al*. 2003 Downey and Beckie 2002).

Therefore, assurance that uninformed recipients will not receive and plant the seed represent an ineffective measure for containment of LL25. Furthermore, some cottonseed fed to livestock may be undigested, reach the soil and germinate. This is a distinct possibility since cottonseed is known to be poorly digested by cattle (digestibility 5-60% depending upon whether the seed was mechanically cracked) (Sullivan *et al* 1993).

While *Gossypium* species are primarily self-pollinated (Wendel, 1995), outcrossing does occur and inter-specific gene flow has been documented in a number of cases (Brubaker *et al.,* 1993; Wendel *et al.,* 1989; Wendel and Percy, 1990). Therefore unintended seed planting will result in outcrossing and hybridization of LL25 with other *Gossypium species.* The risk of outcrossing and hybridization is increased since Africa has 14 species of *Gossypium* and there is evidence of *Gossypium barbadense* becoming weedy (Fryxell 1979). The company dossier also states that crossing in the field is unlikely since cotton is mainly self pollinating with cross pollination in the field minimal due to low levels of insects a consequence of high insecticide use. These assumptions of agronomic practices do not represent effective measures for containment. The cross pollination of cotton occurs by bees so distances of more than 1000m may be required to limit plant mediated gene flow to <0.025% (van Deinze 2005).

No data has been presented on the weedinesss potential of LL25 (studies on fitness, dormancy).

It is unclear from the notification if any environmental monitoring or assessment will take place, as required under the National Environmental Management Act of 1998 (NEMA) and the Biosafety Bill (Bill number 1576), and alignment with the Cartagena Protocol.

In conclusions, due to the lack of Biosafety measures for containment of imported seed and the negative affects on livestock health, it is recommended that LL25 be rejected.

CONCLUSION

We are vehemently opposed to Bayer's application on socio-economic grounds. Approval will mean the dumping of cheap subsidised GM cotton on the South African market and in so doing, substitute the SADC countries with the US, as South Africa's main cotton trading partner. This will destroy the livelihoods of millions of Africans in the sub-region.

Ably assisted by Bayer, which already makes a killing selling agrochemicals in Africa, the entry of cheap, subsidized US GM cotton on the South African market will inevitably find its way to other markets in Africa, with devastating consequences for rural livelihoods of the region as a whole.

Our independent risk evaluation of Bayer's application has revealed that Bayer's GM cotton poses unacceptable risks to human and animal health and the environment. We strongly recommend that Bayer's application be summarily rejected.

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