

## 2006 AEIC Spring Meeting Minutes

P.L. Hunst, Secretary

The 2006 AEIC Spring Meeting was held at the National Weather Service Training Center in Kansas City, MO and was hosted by USDA GIPSA.

### **AEIC Business Meeting**

Secretary's Minutes of 2006 Fall Meeting: A motion was made, seconded and voted positively to approve the Secretary's minutes.

### Treasurer's Report (presented by D. Grothaus in D. Layton's absence):

The current balance in the AEIC treasury is \$19,958. Total dues revenues are projected to be \$8100 due to several members dropping out of the organization/merging. Expenditures are projected to be \$11,645 which would leave a total balance of \$16,483.

There are currently 14 large company members, 10 small company members and 1 individual member.

2006 Fall Meeting: The Fall Meeting will be held on *September 13-14* in Portland, ME and will be hosted by EnviroLogix. For those interested in coming in early, a golf outing will be arranged for the afternoon of Sept. 12. EnviroLogix is looking into a "lobster cruise" as a possibility for the group dinner on the evening of Sept. 13. The cost would be \$48/person. None of the AEIC members present voiced any concern on the cost, however, to reserve the cruise, a guarantee of 25 people would be given, i.e., if 25 people did not go to the dinner, then AEIC will have to pay the difference.

Possible topics for the meeting were proposed. These included: a session on new or alternate technology platforms (microfluidics, nanotechnology, mass spectrometry, field compatible PCR, proteomics, LFS readers, etc.); biotech in small crops (biotech vegetables, regulatory issues for non-commodity crops, transgenic flowers); diagnostics for quality traits (NIR, etc.); certified reference materials – how to acquire them and from whom; PCR instrumentation variability (what to do when companies retire models, what are Stratagene and Roche developing); another talk on plant-made pharmaceuticals (Ventria?); detection of allergens – EU labeling requirements; mycotoxin reduction in transgenic crops; differences in endogenous genes in corn. If members have any other suggestions, please contact Doris Dixon, VP of AEIC.

Updating of the AEIC By-Laws: R. Shillito (President) had gone through the AEIC By-laws and proposed updated language in various sections. These proposed changes were circulated to the membership prior to the meeting. During the meeting, R. Shillito distributed a table of all the suggested changes to those members present. A motion was made, seconded and voted positively to consider all the changes together and then vote once for their acceptance. A discussion was held during which one wording change was recommended for the change to paragraph 5.8: The sentence "It shall be necessary give any notice of..." be changed to "It shall be necessary to give ~~any~~ notice of..." A motion was then made, seconded and voted favorably to accept all the changes to the by-laws.

2006 Goals and Activities: During the 2005 Fall Meeting, a suggestion had been made that AEIC consider doing a study to generate results for the comparability of known samples values derived via PCR and protein tests. USDA GIPSA and ISTA may already possess this data and if not, AEIC members might consider conducting a study to generate the data. It was decided that D. Dixon would query ISTA to see if we could have access to their data and USDA GIPSA would look at their data. At the 2006 Fall Meeting, AEIC will then weigh the options and decide the next step forward.

Another activity that had been suggested from the 2005 Fall Meeting was the standardization of the lateral flow strip tests inserts, i.e., what information and type of information should be included irregardless of the manufacturer. Since M. Bandla has moved into a government position, D. Grothaus (EnviroLogix) has

volunteered to head this effort. Anyone will to assist Dave, please contact him ([david.grothaus@envirologix.com](mailto:david.grothaus@envirologix.com)).

M Thompson (BioDiagnostics) suggested another project might be to create a tool to organize the data currently in the AgBios database on events to make it more useful, i.e., what events need to be tested for, common genetic elements between events, etc. After much discussion back and forth on the pros and cons, M. Thompson agreed to look into the feasibility of such a project. If anyone is interested in helping Mike, please contact him ([michael.thompson@biodiagnostics.net](mailto:michael.thompson@biodiagnostics.net)).

Another possible project was to look more closely at the CEN standard to change the sampling of GMOs in grain and whether AEIC would consider contributing some funding towards modeling work. R. Giroux, R. Cantrill and D. Dixon will put a proposal together for the next meeting.

AEIC Website Update: The AEIC Board has not yet put together suggested changes. They will work on this and try to make some progress prior to the 2006 Fall Meeting.

2007 Spring Meeting: BioDiagnostics indicated that they would consider hosting the meeting in the Minneapolis-St. Paul, MN area.

## **Updates**

USDA APHIS PPQ (M. Bandla): USDA APHIS is responsible for protecting and promoting US agricultural health, administering the Animal Health Welfare Act and carrying out wildlife damage management activities. USDA APHIS PPQ mission is safeguarding US agriculture. PPQ has two regions – east and west. The CPHST portion of PPQ develops and validates methods. The Plant Health Program portion includes the Plant Safeguarding & Pest Identification (of which M. Bandla is the director), the Quarantine Policy Analysis & Support, the Phytosanitary Issues & Management and the Veterinary Regulatory Support. The Plant Safeguarding & Pest Identification unit includes the National Identification Services, Plant Inspection Support and Policy, CITES Policy and Support, Post Entry Quarantine, Plant Germplasm Screening and the Beltsville Inspection Station.

USDA GIPSA (R. Jenkins): GIPSA is developing a validated PCR method for Mon810. In GIPSA's recent proficiency data, it was noted that labs using the IRMM reference material historically under report the Mon810. GIPSA conducted a study in which 3 samples of Pioneer corn were fortified with 0.1 to 3% of all commercial corn events as well as Mon810. Samples were also made using the IRMM reference material. Depending on which reference material was used, significantly different results were obtained. The starch synthase amplification in IRMM material vs. the Pioneer material was 1 to 0.84. If only the IRMM material was used as the standard, a ratio of 1 (IRMM) to 1.9 (Pioneer) was observed. These preliminary results suggest that there is a low bias in the method which is in agreement with other labs using the IRMM reference material.

Protein Paper (D. Grothaus): The AEIC protein paper was submitted to the JAOAC in Oct05 and was rejected. AEIC talked with the editor since the reviewers' comments were not substantial justification for rejection and the editor agreed. The paper was resubmitted and has now been accepted for publication. The AEIC membership voted favorably to pay the consultant to write and submit short articles on the paper in trade journals.

Certified Reference Materials in Japan (D. Dixon/R. Shillito): Japan wants to produce their own source of certified reference materials. They have developed their own PCR methods using plasmid constructs and they are not willing to use the currently publicly available certified reference materials. The technology providers are concerned about having duplicate sources of certified reference materials and concerned about Japan regulators using the certified reference materials in their private companies to fulfill the requirements of the government.

China ILSI/AEIC Workshop (R. Shillito): An update was given by R. Shillito on the jointly sponsored ILSI-AEIC Workshop in China in December, 2005. Approximately 90 people attended the workshop

which included representatives from the Chinese government as well as representatives from the large food companies (Nestle, Unilever, etc.). There were also 22 students from 15 different Chinese institutes. The “learnings” for the organizers of the workshop included:

1. Need to get the message out the first day of the workshop as non-laboratory participants generally attend only the first day
2. Take care when using products from other distributors, i.e., Qiagen kit was marked as containing “dangerous chemicals” which made it difficult to import
3. Will make sure that the AEIC logo is properly displayed as a workshop organizer
4. Need to do some “succession planning” for speakers

USDA AMS (M. Sussman): AMS National Science Lab (NSL) is currently working with AOCS to provide funding for the proposed new ISO TC34/SC16 subcommittee on biomarker analysis in food. NSL is still providing fee-based GM testing and varietal analysis on seed, fruit, vegetables and other commodities. NSL is working jointly with PVPO and UPOV on new methods for molecular determination of new plant varieties for plant variety protection awards. NSL will be hosting a seed training workshop on PCR.

ASTA/ISTA (D. Dixon): ISTA has posted criteria for lab accreditation around biotech on their website ([www.seedtest.org](http://www.seedtest.org)).

Codex CCMAS (R. Shillito): Comments have been sent to USDA (D. Kendall) by some members. The document will probably go back for another round of review.

ISO TAG (R. Shillito):

- In the general document, a request was made by the USA to remove the reference to the sampling standard. Germany had substituted the CEN technical specification and the US protested. The TC34 secretariat has been dissolved so there is no way to resolve the issue at the moment.
- An international forum to discuss sampling needs to be organized.
- A recommendation has been made to ISO for a new Subcommittee on Bioanalytical Methods. Funding of \$20,000 is needed.
- The technical specification (TS21098) for PCR has not yet been triggered. A method will need to be submitted to trigger the formation of an expert working group.
- For the protein standard, D. Grothaus will look at the document to see if anything further is needed for lateral flow tests or ELISA kits.
- For TC34, Hungary has given up the secretariat so a new one is needed. An effort is being put forth to obtain the funding (\$0.6M/yr) from the US so the secretariat would be based in the US. Otherwise, the secretariat may go to the EU or China.

## **PRESENTATIONS**

### **GIPSA Technical Services Division (D. Funk):**

The role of USDA GIPSA is to “facilitate the marketing of US grain” by protecting the integrity of the US grain and related markets through the promotion of accurate testing and mandatory export inspection and weighing. The mandatory export program ensures accurate and reliable quality and quantity assessments via stowage examination and certification.

Global forces are driving change in the grain industry. These forces include 1) higher consumption and production by developing countries, 2) increasing global competition for the grain markets, 3) increasing sophistication of grain buyers, 4) increasing importance of specialty markets, 5) environmental impact concerns, and 6) ongoing developments and debate over acceptability of biotech grain. These global forces are driving changes in grain quality assessment. These include: 1) from grades to grades + functionality, 2) from subjective to objective measurements, 3) from Federal to private official export (with Federal oversight), and 4) from manual to automated inspections. The goals for these new assessments are 1) to enable incentives for producers and grain handlers to maximize desirable traits, 2) segregate and direct grain to

specific end-uses where its value is greatest, 3) improve competitiveness of US grain and 4) to not make it “just another discount factor”.

Quality measurement and the associated costs must be practical at every point in the supply chain. The reproducibility risk must not overwhelm the value. The criteria for choosing the measurement technology include multi-functionality, measurement time and labor input, reproducibility, accuracy and compatibility with the operating environments. The steps to establish functionality include 1) achieving consensus on the definition, 2) a reference method, 3) a suitable technology for a practical method, 4) a robust method, 5) practical standardization, and 6) ability to implement for routine analysis.

The National Conference on Weights and Measures (NCWM) develops industry consensus on the specifications and tolerances for measurements that are the basis for payment. They provide standardized method evaluations and an on-going calibration verification program. Every state has the right to set up regulations for grain trade. To prevent chaos, the NCWM unifies the regulations among states in order to simplify the regulations. USDA GIPSA serves as the sole reference and evaluation lab for grain quality measures.

USDA GIPSA’s future goals are 1) to improve the ability to differentiate end-use quality attributes throughout market channels, 2) maintain a strong and reliable official inspection system, and 3) expand outreach efforts to harmonize quality assessment protocols throughout the US and globally.

#### **Use of GC Testing for a Food Quality Trait – Low Lin Soy (P. Guy, Monsanto):**

Vistive soybeans are the first product in Monsanto’s portfolio for oil modifications. Vistive soybean oil is a low lin oil which as <3% linolenic fatty acid, is a more stable oil, blends with other oils and performs well in frying and spray oil applications. Soybean oil, in general, represents two-thirds of the food oil consumed in the US. The US FDA has recently issued a labeling directive that stipulates that the trans-fat amount in a food must be stated on the label. Major food manufacturers are reformulating their brands to lower the trans-fat content. They have a strong desire to avoid saturated fat, especially that which is derived from the use of tropical oils such as palm oil or coconut oil.

At Monsanto, the Seed Quality Assurance group assures the germination quality, the varietal purity, trait purity and performs compositional testing. For Vistive soybeans, the compositional testing is accomplished through the use of gas chromatography (GC). GC is fast, reliable and reproducible. The method is completely automated and 90 samples/GC instrument are processed per run. The fatty acids are extracted from the soybeans and then the GC separates the methyl ester derivatives of the fatty acids (called FAME products) by the use of a flame ionization detector. The five major fatty acids (palmitic, stearic, oleic, linoleic, linolenic) are separated. Check samples are run daily and plotted on process control charts. These charts show if the process is “out of control” based on the standard deviation and 95% confidence levels.

For the future, new technologies are being investigated since GC is not amenable to a field situation. One of these technologies is near-infrared (NIR) imaging which would be amenable to high throughput screening as well as being nondestructive testing and providing portability of the testing.

#### **Animal Health Vaccines: Use of Plant-Made Pharmaceuticals (M. Pfannenstiel, Benchmark BioLabs):**

Animal health vaccines are regulated by USDA APHIS CVB (Center for Veterinary Biologics) under the Virus, Serum Toxin Act (1913, 1985). The Federal regulations are listed in the Code of Federal Regulations, Title 9 (also referred to as 9CFR). Policy decisions are communicated via Veterinary Services Memoranda and practices via Veterinary Biologics Notices and Supplemental Assay Methods (SAM). Under Title 9 Animals and Animal Products Subchapters A-L, Subchapter A refers to animal welfare and Subchapter E refers to viruses, serums toxins and analogous products, organisms and vectors. Vaccine products must be safe, efficacious, potent and pure.

The CVB is responsible for policy, evaluation and licensing (PEL) which means they license products, define pre- and post-testing guidelines and reagent production and shipping guidelines. CVB also has an Inspection and Compliance component which oversees serial release, inspections, exports, and pharmacovigilance. Veterinary Services (VS) via the National Centers for Import and Export (NCIE) handles the transport permits for all livestock and poultry pathogens and for the possession, use and transfer of select agents.

Vaccines must be safe, potent, pure and efficacious. Safety is measured via safety field trials in which the target species (200-400 animals per site) at a minimum of three sites (differing in geographical location) are tested. Pre-licensing serials are used and the animals are monitored for adverse effects. Field trials are one of the final studies performed prior to licensure by CVB.

Purity is determined by the master cell stocks and working cell stocks being pure cultures or free of extraneous agents. The final product must be sterile or meet defined CFUs for oral delivery. The purity testing guidelines are described in 9CFR and SAMs.

Potency for killed or recombinant components is generally measured by ELISA using a polyclonal antibody for capture and monoclonal antibody as the detector antibody. The monoclonal antibody is specific for the protective antigen. Other assays that are used to support ELISA are western blots and biological assays. The reference antigens that are used range from purified antigens (protective viral protein) to completely assembled vaccines.

Efficacy is measured by the use of clinical models – vaccinated animals demonstrate disease reduction or prevention upon challenge. Some clinical models are described in 9CFR. Dose is defined by the analytical method that measure the *in vitro* potency. *In vitro* potency is generally determined by ELISA to determine the ug protein/mL in the vaccine. The vaccine is then administered to the target species. ELISA is then used again to determine the ug protein/dose. Assays which have been developed to measure the response in vaccinated animals (seroconversion) are ELISA, hemagglutination inhibition and serum neutralization assays.

For immunoassays, there are common problems which include: 1) reference antigen is not tested (validated) in the same matrix as the experimental antigen (expression system); 2) the antibody used in the assay may be produced to a separate matrix (with adjuvant) from the reference or expression system; 3) the antigen and/or antibody have not been qualified for stability, concentration, biochemical or biological features. These problems result in the poor correlation of the reference antigen to the expression system matrix at optimum binding conditions of the antibody used in the assay, i.e., the antibody is not binding optimally to detect the target antigen. Assay validation is necessary to support production, serial release quality control and vaccine monitoring. The parameters of the validation include sensitivity (LOQ, LOD), specificity, accuracy, precision, ruggedness, stability (reference antigen) and dilutional linearity.

For vaccines, stringent validation of the assay is a necessity and protein quantification based on stain binding (e.g., Bradford) or immunoreactivity (e.g., ELISA) may not always be accurate due to degradation, aggregation, etc. For product quality control, it is desirable to have a fast and reliable *in vitro* assay method to measure quantity.

Dow AgroSciences LLC recently received a license for the first plant-produced vaccine. The vaccine was produced in tobacco cells in cell culture and is effective against the Newcastle disease in chickens. Benchmark Biolabs collaborated with Dow on the feasibility, development and manufacture of the serials. Plant cell-produced vaccines are produced in recombinant plant cells and express multiple antigen types. The advantages of the vaccines are that there are no animal origin ingredients, no live or infectious materials in the final product and the cells are grown in a contained system.

### **Corn Breeding 101: What is really going on? (K. Walk, Monsanto):**

The general definition of breeding is the intentional manipulation to plant species to achieve genetic improvement for human benefit. The parameters for genetic improvement include: yield, standability, dry

down rates, disease resistance, insect resistance. Additional parameters may include herbicide tolerance, drought resistance, oil levels, lysine levels, ethanol production, etc.

Modern corn breeding came about with the rediscovery of Mendel's laws in 1900. In 1908, Shull developed the initial inbreds, however, these were weak and inviable. Jones, in 1918, started the hybrid corn revolution by formulating the double-cross hybrid concept utilizing four inbreds. Today, the general breeding scheme for hybrid corn is:

- Year 1 – choose parent and cross
- Year 2-6 – selfing and develop inbreds and make hybrids
- Year 7 – advanced trials, commercialize; success rate is <1%

Sixty percent of the yield improvement in corn is due to genetic improvement vs. agronomic practice improvements. Gains are associated with the improving of the plants' ability to retain yield potential while plant populations and environmental stresses are increasing. The environment has an impact in determining which breeding lines or hybrids perform the best.

Industry investment in corn breeding has increased three-fold from 1960 to 1992. Marker assisted breeding is employed more. Marker assisted breeding utilizes DNA markers which are differences in DNA sequence that are easily identified in the lab. The markers are used in genetic mapping by associating the trait and a marker. This technology assists in advancing the learning about the effects of specific chromosomes and genes that are the key to future yield gains. Marker assisted breeding helps to predict which seedlings breeders will want to select without having to measure the performance of the seedling or that of its parents. Other breeding methods include backcrossing to incorporate non-transgenic traits into germplasm (male sterility); forward breeding – base germplasm carries specific traits while developing new inbred lines; and di-haploid methods – reducing the chromosome number to the haploid state and then double to recover a pure line.

Lab testing of seed does not improve purity. Grow-outs were first purity test and are still the official measure of purity. Isozymes are used as an early indication of selfs, outcrosses or mixtures. Transgenic seeds are tested by ELISA or lateral flow strip (LFS) immunoassays for the presence or absence of the trait. Herbicide tolerant seeds are tested by the towel test in the presence of the herbicide or by planting in the field and spraying with the herbicide. PCR testing is performed to detect any adventitious transgenic events.

For the future, marker-based breeding improvements will continue and a better understanding of yield genes is needed. Global acceptance of transgenic technology is also needed.

#### **MEMBER PROFILE: BioDiagnostics (M. Thompson)**

BioDiagnostics is celebrating their 10<sup>th</sup> anniversary. The company was founded in 1996 and is still privately owned by Quentin Schultz. In 1997, the company acquired its first big customer for ELISA testing. Analytical chemistry testing and DNA testing capabilities were added to the company in 2000. In 2001, a significant contract with a large customer was signed and the company was moved to River Falls, WI into a 20,000 sq. foot facility which is 30 miles from the Minneapolis-St. Paul, MN area. In 2005, the company had 67 employees, 300 accounts across the US and 39 accounts outside the US. The mission of the company is to protect and enhance the value of the world seed market by developing and licensing tools and also developing test plans for seed companies. BioDiagnostics provides web-based access to data for customers.

#### **Packaged Food Labels: Industry Efforts to Affect Consumer Choice (J. Collins, Solae):**

Food labels are regulated by the Federal government who regulates the type of information and the style that it is presented on the food label. Food labels also contain voluntary label elements that are dictated by a company's policy. The main elements of a food label are the product name, the manufacturer's information, the ingredient list, package content (net weight) and the Nutrition Facts panel. Outside of the US, the label also delineates the process by which the ingredients were, i.e, GM or not.

The nutrition labeling has two components—mandatory and voluntary. For the mandatory portion, the label needs to indicate the standard serving size and an expanded list of required nutrients. Voluntary nutrition labeling deals with health, nutrient content and structure/function claims. Nutrient content claims are eye catching and in the case for Solae, a soybean ingredient manufacturer, identifies the product as containing soy protein. Nutrient content claims must be based on fact. For example, the heart symbol effectively communicates the link between soy protein and heart health. Although a product may have a nutrient claim, the consumer must still be convinced that the product tastes good. Two ways to do this are 1) in-store samples and 2) trial size packages.

For marketing a product, a company must show that a marketplace exists and it must have great tasting products—not just “prototypes”. The product should show a consumer benefit and assurance that the product is safe. The general press has been generally negative towards transgenic products outside the US. A couple of strategies for overcoming some of this is use health care professionals to attest to the safety, educate the educators and show continued support to research. When developing a product, should start with what the consumers want rather than developing the product first, registering it and then passing it on to the consumer for use.

### **Claims for Food and Dietary Supplements (M. Wertzberger, Arent Fox):**

Dietary supplements are a class of foods which can make certain claims and FDA has no jurisdiction over. The dietary supplement label is similar to the label for conventional foods with the following differences: statement of identity, structure/function claims and the supplement facts panel.

A label is anything on the package, however, labeling is anything that accompanies an article at any time while that article is in interstate commerce or held for sale after shipment. Advertising is regulated by the FTC.

The Nutrition Labeling & Advertising Act (NLEA) of 1990 made it a requirement for nutritional labeling on all non-exempted conventional food and dietary. FDA is considering making a change on the nutrition panel on the labels. Previously, they were concerned most about calories from fat. This led to the development of “low fat” foods, however, these foods often did not have a lower caloric content. FDA is now concerned about sugar content of foods and are considering eliminating some of the information concerning fats.

There are two types of label claims—nutrient content claims and health claims. For nutrient content claims, all claims must conform to nutrition labeling regulations. An express claim is a direct claim about the level of a nutrient in the food. An implied claim suggest or implies, e.g., “high in oat bran” implies high in fiber. The nutrient content claim must be made in accordance with FDA regulations.

Health claims are any claims made on a label or labeling of a food, including a dietary supplement, that expressly or by implication characterizes the relationship of any substance to a disease or health-related condition. A disease or health-related condition is defined as damage to an organ, part, structure or system of the body that impairs proper functioning (heart disease) or a state of health leading to dysfunctioning (hypertension). There are two types of health claims: authorized and qualified. Authorized health claims must meet significant Scientific Agreement Standard and/or be based on an Authoritative Statement of a Government Body. Qualified health claims can be made by meeting a lower standard for supporting evidence. Permits for qualified health claims are based on varying degrees of evidence and FDA has established a system for ranking the evidence supporting a claim. Recent FDA guidance allows qualified health claims for foods as well as dietary supplements. Qualified health claims are acceptable as long as the claim is the subject of a health claims petition, the scientific evidence supporting the claim is strong and consumer health and safety is not threatened. The FDA ranking of evidence is:

B = moderate to good level of comfort that claim is valid

C = low level of comfort that claim is valid

D = extremely low level of comfort that claim is valid

The authorized statement of support may claim a benefit to a nutrient deficiency disease; may describe general well-being from consumption of a nutrient or dietary ingredient (e.g., garlic); the role of the nutrient is intended to affect structure/function (e.g., calcium for bone strength). The claim may not bear statements to diagnose, mitigate, treat, cure or prevent a specific disease or class of disease.

The food or dietary supplement manufacturer is responsible for substantiation of the claim. There is no defined level of substantiation, however. At least two adequate and well-controlled studies must be submitted. The FDA disclaimer ("This product has not been reviewed by FDA.") must be on dietary supplements with health claims, however, food bearing such claims need not bear this disclaimer.

FDA's final rule on structure/function claims is unclear as to whether these claims are permitted for food but it is generally believed that it can be done. The types of claims for structure/function include over-the-counter monograph claims such as those which claim to have a benefit on occasional or transient conditions such as sleeplessness, acne, etc.; life phase claims such as for pregnancy or menopause. The definition of disease applies to structure/function claims.

### **Health-Related Claims (A. Roberts, Cantox):**

Substantiation of health-related claims is not defined in FDCA. There are no standard protocols for structure/function claims. FDA applies the standard for competent and reliable scientific evidence, which is consistent with the FTC standard for advertising claims. FDA has published draft guidance for dietary supplements.

The guidance document indicates that following parameters must be met in a submission: meaning of the claim, relationship of evidence to the claim, quality of the evidence and totality of the evidence. The meaning of the claim is that the expressed claim should equal the implied claim, i.e., the overall message must be substantiated. The relationship of evidence to the claim means that the substance that is the subject of the study should be the same as the substance that is the subject of the claim. Endpoints measured in a study should be the same as in the claim and the target population should be similar to that used in the study. The quality of evidence means the evidence should be derived primarily from human studies, with intervention studies providing more persuasive evidence than observation studies. Studies should be assessed for bias, confounders, etc. Animal and *in vitro* studies, testimonials and other anecdotal evidence, meta-analyses and reviews would be considered corroborative information only and alone would not be adequate to substantiate a claim. The totality of the evidence refers to the quality, quantity and consistency of the evidence. The level of proof should only be considered valid if the evidence in support of the relationship outweighs the evidence against it (weight of evidence approach). In contrast to health claims, the studies do not need to be published.

The process for review/approval is referred to as SSA (significant scientific agreement) which means there exists a high level of confidence in the validity of a substance-disease relationship, a consensus among qualified experts exists that the claims are true or valid, and that the claims are well-established. The steps in SSA include: identification of all relevant data, evaluation of the studies, evaluation of the totality of the evidence, and assessment of the evidence. For identification of all relevant data, all data must be submitted and human studies are a prerequisite. Data from animal studies alone are insufficient. The hierarchy of human studies is experimental studies (double blind studies) and observational studies. Observational studies include prospective cohort, retrospective cohort, case-control, cross-sectional and case studies. In some cases it is not possible or feasible to do an intervention study for various reasons. With food, double blinding is not always possible. Also, diseases with a low frequency would require a very large sample size. There may also be long delays between dietary exposure and the onset of the disease. Unqualified claims have been approved solely on observational studies. For example, the claim that a low fat diet may reduce some cancers gained approval with 50 observational studies only.

The evaluation of studies is based on assessing the study group sample size, the appropriateness of the controls, adequacy of exposure duration, background diet and other relevant lifestyles, matrix that the food



component was administered, monitoring of subject compliance and the statistical methods. The evaluation of the totality of evidence is an examination of the number and overall quality of the studies as well as the consistency of results across different setting and types of populations.

The attainment of SSA is based on a strong, relevant, consistent body of evidence. Evidence should be available to qualified experts (published in peer-reviewed journals). SSA also takes into account written published statements by experts and documentation of opinions of expert panels, etc.

Qualified health claims utilizes the same process and is reserved for claims that do not meet FDA SSA process.

### **Development of Agricultural Crops with Improved Nutrition and Health Profiles (B. Chassy, U. of IL):**

Two billion consumers live on <\$1 per day and two billion more consumers have more choice but do not live on much more. There will be shortfalls in cereal grain production in the next 20 years since the pressure on land (i.e., development for homes) is mounting.

The process by which a crop is produced is not important for assessing safety—composition is the important factor. There has been no risk or hazard identified to date with transgenic crops. There should be more concern about crops produced via traditional breeding methods since there is greater opportunity to alter composition.

Unintended effects have been the major focus of the critics of transgenic crops. In 2004, Cellini, et al. published a study on unintended effects and their detection in transgenic crops. The conclusion of the study was that the unintended effects were the same as in conventionally bred crops and that transgenic crops were less prone to unintended effects. There have been many negative messages to consumers about the unhealthiness of food from transgenic crops, however, none of these messages have been proven by the research to date.

For nutritionally enhanced foods, the currently employed principles of food safety assessment are sufficiently robust and fully applicable. There are no new science needs. However, two new questions should be asked. These are: 1) is the intervention efficacious? and 2) does it improve nutritional health? Creating a market niche and communicating benefits for any new product is always a challenge.

Soybeans lower serum cholesterol and are a good source of protein. There is also a positive consumer perception of soy. However, soy protein has off-flavors, unattractive color and make chalky protein suspensions plus they are not commonly eaten in Western cultures. Soy is used mainly for animal feed. In the US, 27 billion pounds of soy oil/year is used. Soy oil has a 65% market share. Trans fats are those oils with double carbon bonds and the content of linolenic fatty acid in an oil is most likely to make it high in trans fats. This is why new oil products have appeared with low lin content. New oils are in research programs such as the third generation oils which will have saturated fats removed via transgenic technology. Omega 3 soy and canola oils are transgenic products currently in research. Research is also being conducted on beta-conglycinins to improve their flavor, bind less color pigments and act more like casein in milk.

In summary, crops that offer direct benefits to consumers are here and more are in the pipelines. Developing countries have real needs and transgenic crops may help. The public environment for transgenic crops is still “tough” and it is not yet clear whether science and sanity will prevail.