



Evaluating biological variation in non-transgenic crops: Executive summary from the ILSI Health and Environmental Sciences Institute workshop, November 16–17, 2009, Paris, France

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ABSTRACT

The International Life Sciences Institute Health and Environmental Sciences Institute Protein Allergenicity Technical Committee hosted an international workshop November 16–17, 2009, in Paris, France, with over 60 participants from academia, government, and industry to review and discuss the potential utility of “-omics” technologies for assessing the variability in plant gene, protein, and metabolite expression. The goal of the workshop was to illustrate how a plant’s constituent makeup and phenotypic processes can be surveyed analytically. Presentations on the “-omics” techniques (i.e., genomics, proteomics, and metabolomics) highlighted the workshop, and summaries of these presentations are published separately in this supplemental issue. This paper summarizes key messages, as well as the consensus points reached, in a roundtable discussion on eight specific questions posed during the final session of the workshop. The workshop established some common, though not unique, challenges for all “-omics” techniques, and include (a) standardization of separation/extraction and analytical techniques; (b) difficulty in associating environmental impacts (e.g., planting, soil texture, location, climate, stress) with potential alterations in plants at genomic, proteomic, and metabolomic levels; (c) many independent analytical measurements, but few replicates/subjects – poorly defined accuracy and precision; and (d) bias – a lack of hypothesis-driven science. Information on natural plant variation is critical in establishing the utility of new technologies due to the variability in specific analytes that may result from genetic differences (crop genotype), different crop management practices (conventional high input, low input, organic), interaction between genotype and environment, and the use of different breeding methods. For example, variations of several classes of proteins were reported among different soybean, rice, or wheat varieties or varieties grown at different locations. Data on the variability of allergenic proteins are important in defining the risk of potential allergenicity. Once established as a standardized assay, survey approaches such as the “-omics” techniques can be considered in a hypothesis-driven analysis of plants, such as determining unintended effects in genetically modified (GM) crops. However, the analysis should include both the GM and control varieties that have the same breeding history and exposure to the same environmental conditions. Importantly, the biological relevance and safety significance of changes in “-omic” data are still unknown. Furthermore, the current compositional assessment for evaluating the substantial equivalence of GM crops is robust, comprehensive, and a good tool for food safety assessments. The overall consensus of the workshop participants was that many “-omics” techniques are extremely useful in the discovery and research phases of biotechnology, and are valuable for hypothesis generation. However, there are many methodological shortcomings identified with “-omics” approaches, a paucity of reference materials, and a lack of focused strategy for their use that currently make them not conducive for the safety assessment of GM crops.

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Introduction

Since the first agricultural product produced through biotechnology was introduced to the market place in 1995, many similar crops have sought global, regulatory approval. These products have been carefully evaluated for their overall safety from an agronomic, environmental, performance, and equivalence perspective, including specific assessments of safety for the novel proteins. One aspect of the protein safety evaluation is the question of potential allergenicity.

Approaches to identifying potential food allergens for purposes of safety assessment have been developed and modified over the past 15 years. These approaches were first based on the safety assessment process outlined by Metcalfe et al. (1996) which followed a decision tree approach that relies on gene source, protein homology, Immunoglobulin E (IgE) reactivity, and protein stability. Since that time, the assessment has subsequently evolved into the weight-of-evidence (WOE) approach as recommended by Codex Alimentarius Commission (CAC, 2009). The current Codex recommendations recognize the limitations associated with the specific methods used as part of the WOE approach, and encourage that all suggested methods be scientifically supportable and that additional work be done to clarify uncertainties associated with the methods.

In 2008, the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) Protein Allergenicity Technical Committee (PATC) examined the current state of the science in protein allergenicity evaluation as it applies to products produced through biotechnology (Thomas et al., 2009). One of the conclusions was that endogenous allergen levels in a food may be potentially measured via proteomic profiling approaches. The main limitation associated with proteomics was identified as the lack of background data on the natural variation and range of expression of the many allergens in non-transgenic plants such as soybean that contain more than 20 known or suspected individual allergens.

This lack of knowledge on natural variability led to the decision to hold the international workshop titled “Evaluating Biological Variation in Non-Transgenic Crops,” the outcome of which is summarized in this paper. The focus of this workshop was to bring together scientists from academia, government, and industry to discuss what is currently known regarding the biological variation observed for non-transgenic crops and the methods used to profile the content of hundreds or thousands of analytes in a single sample. The scope of the workshop was intentionally broadened from the relatively few potential allergens that may occur in a crop to a wider array of analytes from fields other than allergy. This was done in order to provide an extensive review of the field and to encourage cross-fertilization between different areas of crop safety

evaluation. Technical presentations and discussion topics included specific focus areas in the molecular, protein, and metabolic sciences, as well as data handling and interpretation. Genetic and phenotypic variability observed in plants within the context of assessing the safety of food crops was also explored.

Summaries of presentations from the workshop’s scientific panel are published separately in this supplemental issue (Table 1). This paper outlines key messages from the presentations, as well as brings forward the consensus points reached in roundtable discussions on eight specific questions posed during the final session of the workshop. A synopsis of the discussion on each question, as well as consensus views, are presented.

The overall consensus of the workshop participants was that while many “-omics” techniques are extremely useful in the research, discovery, and trouble-shooting phases of biotechnology, these analytical tools are not well-suited for regulatory studies of product safety unless the approaches (e.g., proteomics or metabolomics) are targeted to specific safety issues and thoroughly validated for accuracy and precision. More generally, it was agreed that there is little application of the broad profiling techniques and strategies for use in standardized food safety assessments of genetically modified (GM) food crops.

The roundtable format and the focus on the eight key questions promoted significant interaction among the presenters and workshop participants. Summaries of these discussions and areas of consensus are presented below.

1. What near-term role does genomics/proteomics/metabolomics have in support of biotech food safety?

The consensus of workshop participants was that there is currently no role for these techniques as broadly applied survey tools in the safety assessment of GM crops. These technologies in their existing state cannot improve the food safety assessment process which has a long history of being both accurate and robust (e.g., current compositional assessment for evaluating the substantial equivalence of GM crops). It was also agreed that “-omics” technologies at present are most useful as research and discovery tools, although future applications cannot be ruled out as they become more standardized and acquire increased capacity for reproducibility, precision, and accuracy.

Several workshop participants noted that “-omics” tools can measure relative differences in a specific metabolite among two hybrid corn varieties, but that these differences cannot currently be put into the context of biological variation. The biological variation that exists among the thousands of maize cultivars, for example, has yet to be examined systematically. Furthermore, there are no standardized methods and no databases built upon

Table 1

Presentations from the November 16–17, 2009, HESI workshop on evaluating biological variation in non-transgenic crops, Paris, France.

Author and institution	Presentation title
Rita Batista, Ph.D. (National Institute of Health, Portugal)	<i>Plant natural variability: a point to consider in the safety assessment process</i>
William P. Ridley, Ph.D. (Monsanto Company, USA)	<i>Assessing the natural variability in crop composition</i>
Jeroen P. van Dijk, Ph.D. (RIKILT Institute of Food Safety, Wageningen University and Research Centre, The Netherlands)	<i>Gene expression profiling for food safety assessment: examples in potato and maize</i>
Savithiry S. Natarajan, Ph.D. (US Department of Agriculture, USA)	<i>Evaluating natural variability of soybean proteins by proteomic tools</i>
Reiko Teshima, Ph.D. (National Institute of Health Sciences, Japan)	<i>2-D-DIGE analysis of rice proteins from different cultivars</i>
Jay J. Thelen, Ph.D. (University of Missouri, Columbia, USA)	<i>Evolution of seed allergen quantification – from antibodies to mass spectrometry</i>
Ana Sancho, Ph.D. (INRA, France)	<i>Proteomic approaches for qualitative and quantitative characterization of food allergens</i>
David Rouquié, Ph.D. (Bayer CropScience, France)	<i>Investigation of endogenous soybean food allergens by using a 2-dimensional gel electrophoresis approach</i>
Prof. Howard V. Davies (Scottish Crop Research Institute, Scotland)	<i>Metabolome variability in crop plant species – when, where, how much, and so what?</i>
Prof. Bruce M. Chassy (University of Illinois at Urbana-Champaign, USA)	<i>Can “-omics” inform a food safety assessment?</i>

the results from commercial (non-GM) crops to which to compare GM varieties. Therefore, it is currently impossible to describe biologically meaningful differences for most analytes measurable by “-omics” surveys which, therefore, limits the ability to design experiments that could determine biologically significant differences. However, there was agreement that genomics and metabolomics in general could play a role in systems biology to understand plant metabolism. This role would be in the design of the GM product to better understand metabolic processes and to predict functional changes in the context of systems biology, but not food safety evaluation.

Specifically, targeted proteomics may be useful in cases where there are specific questions that can be asked regarding the potential impact on expression levels of endogenous allergens or other groups of related proteins. For example, a targeted analysis of endogenous allergen(s) may be warranted if a transgene is inserted in an allergen coding region of a GM crop. Nevertheless, a better understanding of the biological variation associated with specific proteins and the biological and clinical significance of changes in allergen content are prerequisites before using proteomics as a tool for predictive assessments of risk.

Conclusion: Currently, “-omics” technologies are most useful as research and discovery tools and are thus far inappropriate for safety/regulatory assessment purposes.

2. Can quantitative proteomics lend value to food safety in determining risk for biotech foods without the context of clinical relevance/verification? For example, does it make sense to quantitatively measure soy allergens in crops without first determining allergen thresholds of exposure?

While thresholds of elicitation for IgE-mediated allergy have been reported for some allergens, thresholds of sensitization have not typically been investigated, especially by direct clinical studies of human exposure (Taylor et al., 2002; Taylor and Hourihane, 2008). Workshop participants agreed that from an ethical perspective, it is impossible to consider exposing humans to known allergens for the sake of determining allergenic sensitization thresholds in a specific population. In addition, when elicitation thresholds have been determined and recorded in a given population (e.g., EuroPrevall survey in Europe), they are not typically consistent across geographies (e.g., prevalence of allergy to certain apple varieties is higher in the northern European countries compared to southern European countries; see Goodman et al., 2008), and they can also change with time. When there is a higher exposure for a population to a specific allergenic food, one would expect that there should also be an increase in allergy prevalence. However, this is not always the case, as other factors (e.g., genetics, environment, frequency of exposure) can significantly impact food allergy prevalence. Ultimately, it will always be challenging to marry the limited knowledge of exposure thresholds for known allergens with the rapidly developing technology that facilitates measurement of increasingly low levels of those proteins in foods. Although the ability to measure small quantitative differences among crop varieties is increasing, it will likely remain difficult to place those differences within the context of assessing food safety risk. It should be noted that from a clinical perspective, endogenous food allergens are unlikely to be expressed at substantially changed levels, have limited relevance because patients allergic to the food will normally avoid eating it anyway, and thus the risk to patients allergic to the food will be comparable, whether it is GM or conventional (Goodman et al., 2008).

Conclusion: While small differences in protein levels can be measured, presently, those differences cannot be put in the context of assessing food safety risk.

3. Which (if any) “-omics” technology is perceived as having the most applicability in the near future with regard to building a database of knowledge around natural variability in food crops? Does a central database model (such as the ILSI crop composition database [Ridley et al., 2004]) offer a useful means for the accumulation of data from multiple methodologies and for evaluating natural variability?

Workshop participants agreed that a database would be useful only if there was an understanding of how to interpret data. There was recognition that identifying new data that falls outside the observed data range for a particular parameter in a database would need some accompanying guidance for the biological relevance of that parameter. In other words, as a database includes new parameters, it is important to recognize that it takes time to accumulate enough data to describe the full range of expression for a particular analyte, and that minor differences cannot be extrapolated to infer significance without the complementary background data on exposure. The consensus among participants was that metabolomics has the most applicability in the near future with regard to building a database. From a food safety perspective, the database(s) should be robust, accurate, contain quantitative data, and have well-described methods underlying each parameter. However, this exercise could be very complex given the number of parameters to be potentially surveyed and the number of different evolving technologies that cover the “-omics” field. For example, database standardization is of great importance because the observed variability in a single analyte, if caused by the use of different methods, may not be representative of biological variation. It is envisioned that several databases would be required for different purposes such that research databases may be constructed differently than those used for safety assessments. In particular, because analyses of GM crops rely heavily on evaluations of non-GM reference materials for comparative purposes, a strategy for their analysis would have to be included in building a database for metabolic profiling studies. The ILSI composition database (Ridley et al., 2004) is compiled using data generated with validated standard methods. It is understood that any changes in methods will be well-documented so that users of the database recognize the implication of comparing data based on different methods. Survey methods such as those used for metabolomics procedures typically have not utilized standardized methods and, therefore, individual analytes do not have well-described precision and accuracy, thereby creating a challenge for interpreting this type of data.

Conclusion: Metabolomics has the most applicability with regard to building a robust and accurate database. Such a database should contain quantitative data obtained using standardized methods.

4. Should biotech crops ever be tested exclusively against the non-biotech control (test versus control)? Or, should natural variability always be the baseline against which the biotech crops are compared?

This question emphasizes the challenges in designing safety studies for GM foods, and places particular focus on determining whether the GM food is different from its non-GM control. It is typically considered “out of context” to only test GM versus a single, closely related control variety without understanding how a specific parameter may fluctuate among varieties of a particular species, e.g., hybrid corn varieties vary each year as breeders accommodate the needs of farmers. Workshop participants agreed that few studies have been performed to study the question of how best to assess GM crops in a systematic way with regard to specific parameters. The consensus of the workshop participants, however, was that both approaches are needed in a tiered, two-step

approach. As a first step, GM crops should be tested against their closest non-GM comparator. If differences are found, the changes should then be evaluated in the context of the natural variability of a given analyte in commercial non-GM crop varieties to help understand whether or not the difference observed in the first step is relevant from a biological perspective. Without data on biological variability, it is not possible to fully address the level of change that would be acceptable or its biological significance to the consumer from a safety perspective.

Conclusion: A tiered approach should be utilized: in Tier 1, the GM crop is compared to its closest non-GM comparator. If differences are observed, changes are evaluated in Tier 2 in the context of natural variability of commercial non-GM varieties.

5. Where does the value lie in a global “-omics” analysis versus a targeted approach in assessing GM foods? Does the global or survey approach provide a useful analysis of mode of action for GM traits?

It was understood that a “targeted approach” involved a select set of parameters for which there was fairly good reproducibility and a clear identification of the analytes, as opposed to broad (global) survey strategies in which many parameters (e.g., some metabolites are identified and some are unidentified metabolite molecules) are simply catalogued from a sample. In the case where harmonized methods and databases are available for “-omics” analyses, the advantage of using a global analysis is when the mode of action (MOA) is not known or not completely understood. There was consensus that the most valuable application of “-omics” analyses would be in a targeted fashion wherever complex processes, such as basic biochemical metabolism pathway identification, are understood and are used for product design, product production and characterization, or product troubleshooting. For example, metabolomics may support industrial manufacturing by solving large-scale bacterial fermentation production issues, whereby a metabolic profile can provide an indication of nutrient deficiency. Targeted approaches are also likely best used in biotechnology products to determine when a transcription factor is up- and down regulated at both the transcript and protein levels. This approach could also support safety studies that attempt to describe the limits to which a transgene may affect other genes or metabolic processes. Nevertheless, determining small variances and describing those differences with statistical analyses is not likely to have clinical meaning with regard to safety, especially if natural variability has not been well described.

In the safety assessment of GM foods or other novel food sources, the focus should be on determining the hazard. Thus, a targeted approach to identify and characterize parameters that are important for describing food safety and potential risk is appropriate for this paradigm in cases where the variability and clinical relevance is well understood first.

Conclusion: The most valuable application of “-omics” analyses is in a targeted approach.

6. There will likely be many differences observed with a global approach. How are these to be interpreted? The question of how to interpret data that may be statistically different, but may or may not be biologically relevant, is extremely important. Some questions regarding quantitative measures are:

- What level of precision is meaningful? How much of a change outside of natural variability is a concern?
- Are tolerance intervals useful?
- When does sensitivity of methods (ability to measure low levels) become irrelevant (e.g., ppt, ppm)?

Determining statistical significance between two measures of a particular parameter depends greatly on experimental design, as well as specific knowledge of the expected variability in the parameter and reproducibility of the method used to produce the data. Statistics has become an increasingly important aspect of food safety studies because of the desire to understand the impact of minor differences that are frequently observed as part of large data sets. Workshop participants agreed that the analysis and interpretation of data can be complex. Any analyte can have its precision and accuracy described if it is quantitatively measured. This is important in considering “-omics” because many of the methods have not yet evolved beyond the ability to produce qualitative data and relative comparisons between samples. For validated quantitative methods, various strategies exist for describing assay variability, detection limits, and data ranges which can be used to compare “test” samples against the “normally observed range.” As an example, tolerance intervals could be useful as a statistical method for evaluating potentially significant differences, but should be implemented with an appropriate experimental design.

The limits of detection were discussed due to the typical trend toward ever increasing sensitivity. The concentration ranges at which many analytes can be detected are very low (femtomolar) and can easily exceed the physiological expression level of those analytes in vivo. The point was expressed that the ability to technically measure analytes can eclipse the level of biological relevance, especially in terms of describing the exposure of food components as consumed by humans. For example, the small differences in the content of food proteins among different samples likely have no biological impact on the overall exposure level to those proteins. It was also recognized by the workshop participants that the ability to measure very low concentrations of analytes may increase the probability of generating analytical artifacts, and that balancing the detection limits with the intended use of the data is preferred.

Conclusion: Increase in the sensitivity of the detection methods and the number of endpoints measured trigger many analytical artifacts. Therefore, the biological relevance of small differences in the content of analytes among different samples is decreased.

7. Which method(s) is amenable to standardization and routine testing/high-throughput testing?

Standardization is achievable for any analytical method, although standardizing for routine use among multiple laboratories over years of repeated use remains a challenge for any new technology. Routine testing of large quantities of samples typically requires greater time and money, and might be possible only in larger, well-equipped laboratories. Nevertheless, application of any technology requires validation of its reproducibility and accuracy, especially in considering them for use in regulatory safety studies of biotechnology-derived foods.

7.1. Genomics

Several microarray techniques exist and can be standardized. However, no high-throughput technique is envisaged during the next 10 years, even though cost per sample is being reduced (primarily with the Arabidopsis-focused microarrays). Data analysis remains the most time-consuming and costly aspect due to the fact that several thousand genes can be screened for their relative expression levels in a single sample. In some respects, the inordinate amount of data can be a detriment to answering hypothesis-based studies. Indeed, the technology itself should not be considered the driving force behind study designs.

7.2. Proteomics

The standardization of methods for the extraction of seed proteins is typically the first part of this technology to require extensive characterization and validation. A balance between yield and representation of the target proteins is typically required for the study of multiple proteins in complex matrices. Quantifying proteins by labeling specific peptides can be applied in a targeted approach using sample digestion and LC/MS/MS. Published standardized methods that account for standardizing extractions, describing the technical variability, and assessing data interpretation do not yet exist in a cohesive approach. Furthermore, these analyses tend to be very laboratory-specific which limits their use in a standardized approach. Two-dimensional (2-D) gel electrophoresis is laborious, time-consuming, and expensive. It is likely never to be amenable to a high-throughput process. If this method is coupled with immunoblotting, as is frequently requested for endogenous allergen analysis, the paucity of well-characterized sera is another severe limitation in considering these types of experiments. In fact, analysis of proteins by 2-D western blotting is further limited by the size of the gels, which needs to be relatively large, and, therefore, demands relatively large amounts of sera. As a result, any biological variability that the technique may be able to differentiate is plagued by the variability inherent in the technique itself.

7.3. Metabolomics

These studies can be of very high quality with extensive documentation (i.e., GLP) and produced in high-throughput processes when the samples are relatively uniform in their matrix (e.g., as in urine or blood for toxicological studies). However, in considering study formats used in pharmaceutical drug trials and their potential application to food and food crop analysis, the transformation of these study formats to include metabolomics is difficult to consider until the techniques become standardized across laboratories and throughout the food safety assessment process. It was reiterated that validated standard ISO-type methods which exist for food crop compositional studies do not exist for metabolic profiling studies.

Conclusion: All of the “-omics” technologies have to be standardized before their use. Among the “-omics” technologies, metabolomics is the most amenable to standardization.

8. Would “-omics” approaches be useful or necessary for evaluation of new varieties of plants produced via traditional methods such as mutagenesis or wild-crossings?

An extensive characterization of new plant varieties is standard practice and helps to ensure that neither farmers nor consumers are unduly impacted. These characterization studies include phenotypic studies to determine acceptable plant form and agronomic behavior. The history of the safe-use concept (Constable et al., 2007), which encompasses the phenotypic and agronomic analyses, is sufficient to address safety questions about products such as foods that are produced in this traditional manner. Unlike GM varieties, traditionally bred or mutagenic varieties do not undergo a safety review because they are deemed as not having any different inherent safety risk. The consensus view of “-omics” was that these technologies are not a useful addition to the processes and information base currently used to determine novel food safety. To reiterate, global survey approaches using “-omics” cannot reliably place the data into a context of risk determination unless their natural variability range has been established and the individual parameters (e.g., specific transcripts, proteins, or metabolites) have

been determined to have specific importance to animal or human toxicology, allergy, or nutrition.

Conclusion: “-Omics” approaches are not useful or appropriate for determining novel food safety.

Overall conclusions

“-Omics” techniques are frequently used to survey the response, condition, or associated analyte variability of a tissue, organ, or even whole organism (Lawton et al., 2008). In their broadest applications, “-omics” can detect hundreds or thousands of analytes and measure relative expression levels.

Three technical criteria should be considered in the application and experimental design of “-omics”-based studies of plants/crops. These are considered the basics of design that help define the analyte variability that is considered necessary before moving to hypothesis testing:

1. Does the analysis measure a specific analyte with well-characterized sequence, biochemical, and biophysical information?
2. Can the analyte(s) be measured quantitatively?
3. Can the accuracy and precision of the measurement technique be defined for the analyte(s) of interest?

Utilizing allergenicity as an example, it is likely that the technical criteria for well-defined allergenic proteins can be established by proteomic methods, and that they may be quantified with satisfactory precision and accuracy (see Thelen et al. and Rouquie et al. in this supplemental issue; Table 1). Importantly, it was acknowledged that from an allergenicity perspective, the absence of basic knowledge surrounding what specific physico-chemical properties determine whether a protein is or is not an allergen greatly limits the effective application of a wide variety of technologies for the explicit purpose of assessing product safety, of which “-omics” is one class. A specific “-omics” assessment such as proteomics can survey many of the extractable proteins from a seed. However, broad surveys are not necessarily complete in describing everything that a sample may contain (e.g., proteins with extreme isoelectric points can be left out of a typical 2-D PAGE analysis), and the individual proteins that are detected may not be quantified because the technique does not easily allow for multiple standards and other aspects of a validated assay.

Therefore, “-omics” strategies that survey and show relative differences between samples are limited in their applications to hypothesis testing. Well-established methods with good annotation of their precision, accuracy, and robustness support targeted, hypothesis-driven analysis and are more applicable to the data required in risk assessment paradigms.

Three general guiding principles, though not exclusive to “-omics,” should also be considered before applying “-omics” to hypothesis testing whereby one plant type may be compared to others of similar breeding, agronomic performance, and growing conditions:

1. Does the analyte(s) of interest have any relevance to human or animal safety? If so, are there characterization data that support a dose–response relationship, threshold dosages, no-observed-effect levels, etc.?
2. If the analyte(s) of interest can only be measured qualitatively, can relative comparison data be of any use to food/feed safety assessments?
3. Are there data available that indicate that the analyte(s) of interest changes in expression level due to breeding history/cultivar selection, culture conditions, or abiotic environmental determinants? What is the natural variability of the analytes being measured?

The comprehensive coverage of many analytes by the “-omics” techniques makes it more difficult to meet principle #1, because for many of the measured proteins, there is no knowledge of whether (or current belief that) their presence in a crop is related to allergenic effects. Moreover, establishment of dose–response curves and threshold dosages for allergenic foods is still premature, and there is no clear picture of how the individual components contribute to the overall allergenicity of a crop. The dose–response curves for allergenic proteins do not follow the same dose–response curves as those observed with toxic proteins. Furthermore, although experience with clinical oral challenge trials indicates that exposures do exist below which individuals with confirmed allergy will not experience allergic reactions, this is observed with a limited number of allergens (e.g., Taylor et al., 2002, 2004, 2009; Threshold Working Group, 2008). The problem becomes even larger when looking at genomics, because the relationship between mRNA and protein is non-linear and often unpredictable. As for metabolomics, there is currently no knowledge to indicate whether or not the metabolome influences allergenicity or even how this type of interaction may occur. For principle #2, relative data can play an important role in food/feed safety assessments. In reality, with the exception of proteins (Thelen et al. in this supplemental issue), most “-omics” data will be qualitative in nature. Importantly, the analytes, whether measured qualitatively or quantitatively, should be considered in the context of a targeted, hypothesis-driven approach, natural variability, and their potential impact on safety.

Finally, considering principle #3, it is clear that there is still only fragmentary knowledge of the overall variation in conventional crops and how this may be influenced by environmental conditions. This is not a drawback of the “-omics” methods per se, but is a call for more data collections to be established for conventional crops before the techniques are applied in a regulatory setting.

The question of utilizing “-omics” for food safety has come about as the technologies themselves have evolved to the point where there is a perceived capacity to more easily measure multiple analytes in complex matrices. There is also the perceived need to “hunt” for and more completely describe the potential for unintended effects in foods which are considered a risk of transgenic biotechnology. Yet, GM food crops undergo extensive compositional analyses that have a record of producing safe consumer products. In fact, workshop participants agreed that the current compositional assessment for evaluating the substantial equivalence of GM crops is robust, comprehensive, and a good tool for food safety assessments; it has and continues to provide adequate safety assessment data.

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