U.S. FOOD & DRUG ADMINISTRATION

Foods and Veterinary Medicine (FVM) Research Impact

Advancing Public Health through Regulatory Science

*The **FVM Research Impact** Work Group*

Winter 2017/Spring 2018 Publication

*"There has been heavy dependence on journal metrics [in the research community]. However, [journal] metrics show the reach of the research in terms of how widely it is disseminated and the uptake. **But, journal metrics do not characterize the influence created, such as resulting actions or changes or the manner in which the research knowledge is used**."*

- Centers for Disease Control and Prevention

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ABOUT RESEARCH IMPACT

Traditionally, metrics used to determine the impact of research have been primarily based on the number of times a resulting article has been cited or the relative importance of the journal that published that article. And while this provides an indication of the dissemination of the research, it is limited in its ability to provide the extent of the impact of research; how the research has been used to affect change.

The Research Impact Work Group (RIWG) serves to assist in the provision of collective organizational understanding and assessment of research impact. We serve to bridge the gap between the researcher in the lab. We share the collective desire to find ways to qualitatively – and (in time) quantitatively –express the impact that the research we are doing within the Office of Foods and Veterinary Medicine (OFVM) has on the public health landscape. We exist, essentially to enable meaningful characterization of the breadth and depth of the impact of research that comes out of FVM – and beyond.

WHY IMPACT

The FVM Program's aim is to protect the U.S. food supply and animal health and ensure that cosmetics are safe through data-driven regulatory actions. Faced with a rapidly changing and increasingly complex environment, the FVM Program depends on internal research and methods development to facilitate timely identification and response to product adulteration and to support regulatory decision-making. Our evaluation of the quality of these research efforts, therefore, not only depends on an assessment of the rigor and reliability of the science, but also on an analysis of its contribution to the public health mission of the Agency. The development of a framework for gauging the broader influence of FVM research on public health outcomes underscores the commitment of the FVM Program to good stewardship of public funding. Additionally, we are working to strengthen the Program by highlighting best practices in the effective and efficient translation of research into advancements in public and animal health.

IMPACT FRAMEWORK AND INDICATORS

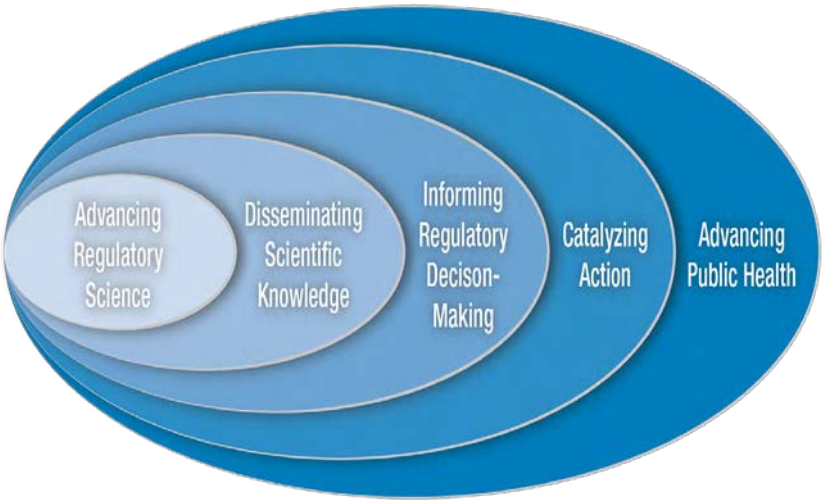
Our Purpose

Under the authority of the Science and Research Steering Committee (SRSC), the RIWG serves to:

- identify what research impact means to all stakeholders in the regulatory research pipeline within the FVM setting and clearly articulate the purpose and benefits of looking at research impact for a variety of internal and external stakeholders;
- create a systematic approach and/or methodology to characterize, demonstrate and communicate the scope, intended and unintended impacts on internal and external stakeholders of FVM regulatory research,
- perform annual retrospective analyses and reporting on research initiatives to understand impact and strategic alignment to identify strategies to enhance the public health impact of FVM scientific research.

The Framework

The shared framework results from the collaborative effort of the founding Impact Work Group and refinement by it's current membership. It is iterative in nature, consists of domains, evolves as necessary and speaks to the continuum that is research impact.



The ultimate goal of public health research is to improve the health of the public. However, steps need to be taken by the scientific community, regulatory agencies, and external stakeholders to achieve this goal. First, research must be conducted in a manner that addresses a public health need. If the results of the research suggest a solution to a public health need, the research must be disseminated so it can be reviewed, discussed, and accepted by scientific and non-scientific communities. If the research is accepted, regulatory agencies can use the information to inform decisions on how to address the public health need. This could include creating or amending regulations or working with stakeholders to develop voluntary actions. The actions taken, based on promulgated regulations or voluntary initiatives, will hopefully help to improve the health of the public.

This framework can also be used to make decisions about what goes in to our research portfolio. Studies and projects are undertaken to advance regulatory science. These studies are related to predetermined research objectives – created by our centers and the Office or Regulatory Affairs (ORA) to address public health and thus programmatic needs. The studies undertaken align with our strategic plans, outcomes are shared or disseminated via internal and external FDA communications, The resulting outcomes enable organizational readiness, process change, and provide evidence necessary for action. These actions can impact consumption and exposure rates, thus advancing public health – both human and animal, which is the core of our organizational mission.

In recent years, the FVM Program has increasingly incorporated risk-based priority setting into strategic planning and resource allocation processes. Both the Centers and ORA now participate in a science and research prioritization process, though the specific criteria for ranking priorities vary by organization. Ongoing research initiatives aligned with established priorities will be evaluated for anticipated impact, with the goal of generating feedback to researchers about how studies may be redirected to optimize impact. This work will also function as a validation step for the Impact Framework.

OPERATIONALIZING IMPACT

As envisioned in the RIWG's paradigm, the continuous process by which past, present, and future FVM research is considered will provide a means for illustrating downstream relevance of prior or completed efforts undertaken and for guiding the efficient utilization of FVM research in future activities. To enable meaningful characterization of the breadth of research impact and to identify facilitators of impact, the FVM RIWG, comprised of representation from the OFVM, the Center for Food Safety and Applied

Nutrition (CFSAN), the Center for Veterinary Medicine (CVM), and the Office of Regulatory Affairs (ORA), follows a general framework. The framework is based on literature reviews, collaboration with other agencies and institutions, internal discussions, open ended interview question and answer sessions with Principal investigators and case study analyses.

Indicators of Research Impact

Advancing	• Research findings that address a defined knowledge gap • Research initiative that addresses regulatory actions or needs • Method qualified for use in the field (e.g., method development, validation, and implementation (MDVIP) guidelines. etc.) • Innovative approach to fill a defined need
Disseminating	• Expanded knowledge base on emerging food safety, animal health, and human health/nutrition issues • Data meeting applicable standards of quality • Strategic partnership/collaboration (leveraging FVM's science resources) • Peer-reviewed scientific publications • Reaching intended target audience through a communication plan (e.g., scientific journal audience, via applicable media outlets) • Citations in scientific publications • Citations in grey literature • Presentations at trade meetings, academic conferences, standards organizations, AOAC International, etc.
Informing	• Development or change in inspection and sampling strategies • Development or change in external communication strategies • Policy decisions • Support of compliance and enforcement actions (e.g., contribution to warning letters, etc.) • Contribution to pre-market reviews
Catalyzing	• Adoption and adaptation of research findings by non-regulatory governments and government agencies • Adoption and adaptation of research findings by industry • Influencing change in stakeholder behavior as a result of disseminating scientific knowledge • Technology transfer from FDA to stakeholder groups • Use of research findings in advocacy initiatives • Subject of a professional society meeting • Creating or reorienting partnerships • Removal of hazardous commodity from the marketplace • Reduction in exposure time to hazardous commodities • Reduced frequency and severity of outbreak events • Improvements in consumer understanding of FVM-regulated products
Advancing	• Reduced economic burden of illness attributable to FVM-regulated products • Reduced morbidity and mortality attributable to FVM-regulated products

WHERE HAVE WE BEEN?

The RIWG was formed with the goal of developing a broad-based, flexible framework for assessing the public health impact of FVM research projects and programs. We seek to encourage continued understanding and adoption of the Impact Framework and Research Impact. In support of our goals, we have recently worked together to accomplish the following:

Charter our Work Group. Document RIWG purpose, background, organization and membership, function, roles and responsibilities, procedures and records and gain approval by the OFVM's Science and Research Steering Committee (SRSC).

Finalize Foundational Documentation. Foundational documentation includes, but is not limited to, documents created by founding members, documents that record and explain the Impact Framework, boilerplate communications pieces, etc. saved to the Work Group Foundational Documents SharePoint folder.

Create Standard Operating Procedures (SOPs) for Known Group Processes and Procedures. Standard Operating Procedures include but are not limited to the Annual Case Study Review Process, etc.

To support the Agency-wide shift toward risk-based prioritization and resource allocation, FVM has expanded research tracking and coordination efforts over recent years. Research initiatives are now logged, aligned with prioritized research goals, and tracked through completion. Because outcomes of research are not routinely solicited or evaluated, available outcome data has been somewhat incomplete and unreliable. While the Centers have individually initiated pilot programs aimed at categorizing research, aligning budget with performance measures, and tying research to regulatory goals, evaluation efforts have not yet fully assessed downstream contributions to stakeholder changes in behavior or health outcomes.

Celebrating Impact, Continued Case Study Impact Analysis. This year we spent a great deal of time going through all of the studies submitted in previous years and the studies submitted this year for nomination for celebration. From our analysis, certain studies were deferred for review until the next year or two to allow for the impact of the research to be realized and mature (e.g., publication of a resulting method in the BAM to get the impact ball rolling). What resulted was two mature and impactful studies and one impactful program. There are so many promising studies ripening for impact and the work group looks forward to learning about them. Shameless plug – do share – we'd like to hear from you!

WHERE ARE WE GOING?

While the RIWG, in conjunction with the FVM enterprise, has made great strides in understanding, encouraging, enhancing and celebrating the impact our work has on the regulatory and public health landscape, we have more work to do to ensure that we continue in our current trajectory and maintain momentum.

Revive FDA Impact Forum. The RIWG will reestablish regular meetings of the Research Impact Forum (RIF). The RIF is an FDA organization-wide body with membership from different disciplines, centers and organizations and serves to further promulgate an understanding of how research conducted across CFSAN, CVM, and ORA is making short, mid, and long-term impacts on regulatory science, decision making, FDA stakeholders and partners, and public health.

Expansion to Retrospective and Priority Analysis. Aligning scientific research with FVM priorities is a foundational step toward focusing efforts on initiatives most likely to contribute to advances in public health and regulatory decision making. Given that effective translation of research outcomes into broad improvements in health is a complex and multistep process, even research targeted to high-priority issues may fail to generate immediate impact. Moreover, risk assessment and priority setting are themselves inherently intricate and imprecise processes that require iterative evaluation and refinement. Future phases of work carried out by the RIWG will serve to introduce a broader retrospective review of FVM research portfolios and priorities, intended to identify strategies to enhance the public health impact of FVM scientific research. As such, it is intended in the future that, at scheduled intervals, research portfolios at the office level will be retrospectively evaluated. The output of the review process will be recommendations for enhancing the characterization of impact.

IMPACT SUCCESS STORIES

FVM research is conducted by a productive and talented workforce of scientists across multiple Centers and Offices tackling diverse and challenging scientific issues. The impact of FVM research can be viewed through many different lenses with no one definition of impact conferring more value than another: the impact of a research project will be initially defined by its original goal and intention. This issue features two case studies identified by the RIWG to highlight FVM research and to illustrate a breadth of regulatory research impact.

QUANTIFICATION OF PLANT STEROLS/STANOLS IN FOODS AND DIETARY SUPPLEMENTS CONTAINING ADDED PHYTOSTEROLS: A MULTI-LAB VALIDATION CARTS# IF01227

Cynthia Srigley, CFSAN, PI; Rahul Pawar, CFSAN; Gregory Noonan, CFSAN; Carolyn Chung, CFSAN; Blakely Fitzpatrick, CFSAN; Lowri DeJager, CFSAN; Richard Cantrill, American Oil Chemists' Society (Retired); Steve Hansen, Cargill

Overview and Impact

There is a substantiated link between the consumption of plant sterols and stanols and the reduction of the risk of Coronary Heart Disease (CHD). As such, in 2000, the FDA authorized the use of an associated health claim for industry to use; allowing communication to the consumer that their product could reduce the risk of CHD if the combined weight of the sterol or stanol ester food additive is greather than 80% of the combined weight of the five major phytosterols; (i.e., campesterol, campestanol, stigmasterol, β-sitosterol, and sitostanol). However when the claim was allowed,no method available for ensuring this claim was being used properly.

Image of Fruit, Vitamins and Medication

In order to meet the regulatory need, a method for quantifying phytosterols based on best attributes of existing single lab validated methods was needed, as the only way to validate claims was to require manufactures to keep records. As such, the team took on the challenge of evaluating the performance of this phytosterols method in an international, multi-laboratory collaborative study. The objective of the work undertaken was to evaluate and take from the best methods by which this could be done to create a reliable method for validating the claim. The resulting method was developed, in collaboration with Cargill and the American Oil Chemists' Society (AOCS).

Stakeholders and Study Design

The work was carried out in two phases, a pilot study and a multi-laboratory collaborative study. For the pilot study, two single laboratory validated methods were evaluated for their performances with regard to sample preparation and chromatographic separation of the five major phytosterols that are the subject of FDA's health claim. The best attributes of the two methods were combined to create a new method (AOCS Method Ce 12-16). The method was then tested in a multi-laboratory collaborative study involving 14 laboratories from six countries. Collaborative samples were purchased from stores in the Washington, DC metropolitan area or from online vendors, or they were donated by the industry. Statistical evaluation of the collaborative samples was performed by a statistician from Cargill.

The outcome of the research was a validated method that could be used to support the FDA health claim for plant sterol/stanol esters and the reduced risk of CHD (Interim Final Rule, 2000) for the five major phytosterols.

Aligned Study Indicators of Research Impact

	Preliminary Indicators of Research Impact
Advancing Regulatory Science	• The FDA now uses the method developed in ORA labs for verifying the composition of products that contain added phytosterols and claim the reduction of risk of CHD, where previously there was no validated method available to do so. Manufactures were required to keep records and compliance could not be ensured.
Disseminating Scientific Knowledge	• Initial interactions with Cargill resulted in an FDA, AOCS roundtable discussion to bring new methods to become new methods. Additionally, those involved with the research were kept in the communications loop and in step with the drafting of the updated and final regulation. The FDA and stakeholders wanted to move forward with a full collaborative study, combining two methods into one successful method. The method has been adopted by ORA labs and manufacturers of products of contract labs verifying concentration of products. • With respect to disseminating scientific knowledge, the researchers and stakeholders worked very collaboratively throughout the life of this study – in planning, recruitment and execution. • The methods being combined and validated were published in 2015.
Informing Regulatory Decision-making	• There was previously no official method to validate the allowed claim, and the few methods that were available were not appropriate for quantification of phytosterols in the broad range of products that are eligible to bear the health claim. Additionally, they were not suitable for the analysis of the five major phytosterols which are the subject of the health claim. The outcome of the research was a validated method that could be used to support the FDA health claim for plant sterol/stanol esters and the reduced risk of CHD (Interim Final Rule, 2000) for the five major phytosterols. • Additionally, the project supported CFSAN's Science and Research Strategic Plan Goal to develop faster and validated methods to support regulation. ISO also voted to adopt the method as a standard. • There is, also, the possibility of this developed method to be applied to other areas, such as oil authenticity (although may be costly, at present) and validating application ingredient lists.
Advancing Public Health	• Now that we have a health claim that can be validated through the advanced regulatory science and that has been shared, the possibility for the advancement of public health is possible. Health claims can now be substantiated and are more reliable to the consumer. Additionally, Nutritionist/Dietitians may instruct those with whom they are working to take products with this claim into consideration in their food purchases. • And consequently, Phytosterols may start to show up more and more in the food supply.

DEVELOPMENT OF A MULTIRESIDUE METHOD FOR THE DETERMINATION OF HORMONES IN BOVINE MUSCLE TISSUES CARTS# IV00305

Pak-Sin Chu, CVM, PI; Tricia Johnson, CVM; Sara Sklenka, CVM; Hiranthi Jayasuriya, CVM; Wei Song (now with CDER); Upul Nishshanka (no longer with the FDA); Kande Amarasinghe (now with CDER)

Overview and Impact

Many meat products are now marketed as containing no added hormones. While the joint Food and Agricultural Organization World Health Organization (FAO/WHO) expert committee on food additives (JECFA) and FDA deem a few hormone residues found in meat of treated animals as safe for consumption, the use of hormones in animal meat production is strictly prohibited by the EU and in several other countries. Trade disputes between the European Union (EU) and US regarding hormones have been occurring for many

Image of a Cow in a Field

years. Methods previously developed to ensure there were no hormones present were time consuming, costly and less reliable than desired. Using advances in instrument technology, FDA researchers consolidated two procedures to detect hormones in bovine muscle tissue into one –minimizing analysis time, cost and the potential for errors. The method provides a specific and accurate method to test product. Additionally, the new method enabled the simultaneous determination of sixteen hormones of dissimilar chemical properties in one single step.

Aligned Study Indicators of Research Impact

	Preliminary Indicators of Research Impact
Advancing Regulatory Science	• The work undertaken by the research team advanced regulatory science through the creation of a method that was faster, cheaper and more reliable than previously used methods. A two step process was melded into one and 16 differing hormones, also dissimilar in chemical properties could be analyzed in a single step. Additionally, this method was determined to be fit for use in both cattle and fish, as follow on studies on hormone metabolism were conducted using the method.
Disseminating Scientific Knowledge	• The multifaceted research project that advanced regulatory science led to the publication of four research articles and sixteen presentations on this subject. The research findings were presented at multiple scientific meetings including the Florida Pesticide Workshop, the PacifiChem, and the American Chemical Society Annual Meeting. Additionally, an SOP was developed and disseminated to provide information to laboratories planning to use the procedure to enable successful replication of the method. A member of the research team visited the FSIS Eastern Laboratory in Athens Georgia to train the FSIS personnel. The research team maintained close contact with the FSIS team during the FSIS validation of the method to provide needed assistance to ensure a clean transfer of the method. Perhaps just as importantly, the method was provided to USDA Food Safety and Inspection Service (FSIS) and is currently in use.
Informing Regulatory Decision-making	• As the result of disseminating the advanced regulatory science yielded from this study, FSIS changed their existing sampling strategy. Carcasses are randomly selected for sampling, as the method is designed to detect anapproximately 1% violation rate with 95% confidence. FSIS plans to test 1000 samples covering four classes of animals as part of this program in 2017 data collected serves as a baseline level for chemical residue exposure. Again, this enables compliance with EU import requirements.
Advancing Public Health	• Having the method available has allowed FSIS to verify labeling claims. Many meat products are now marketed as containing no added hormones. Because of the availability of the method, FSIS is now able to check these label claims to ensure that product is being truthfully marketed and exported. While the joint Food and Agricultural Organization World Health Organization (FAO/WHO) expert committee on food additives (JECFA) and FDA deem a few hormone residues found in meat of treated animals as safe for consumption, the use of hormones in animal meat production is strictly prohibited by the EU and in several other countries. Trade disputes between the European Union (EU) and US regarding hormones have been occurring for many years. The method provides a specific and accurate method to test product. The method will provide data needed to address the significant trade and other issues raised by the dispute over the use of hormones.

THE VET-LIRN PROGRAM

Renate Reimschuessel, Director (CVM); Jennifer Jones (CVM); Sarah Nemser (CVM); Jake Guag (CVM); Andriy Tkachenko (CVM); Olgica Ceric (CVM)

In previous publications, only research projects have been celebrated. This year, the view has been expanded to understand the impact of not just research project research activity, but programmatic activity, as well.

Overview and Impact

While not a project, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) program has been having an impact on many of the domain areas we have been discussing today. If necessity is the mother of invention, the Vet-LIRN program is her healthy child. During the pet food recall of 2007, CVM recognized the importance of interactions with groups outside of government, such as the American Association of Veterinary Laboratory Diagnosticians (AAVLD) who reported laboratory results, images of damaged kidneys and even local veterinarians who reported cases (on the phone) and sent actual tissue samples to CVM.

CVM obtained funding in autumn 2010, which came, in part, from funds for the Food Safety Modernization Act (FSMA). to develop a network of labs to facilitate interactions between outside laboratories and the CVM personnel who respond to adverse events.

Image of the Vet-LIRN Logo

The Vet-LIRN Program sits within the Office of Research in the Center for Veterinary Medicine, under the umbrella of the Office of Foods and Veterinary medicine and serves to promote human and animal health by providing CVM with scientific information – either through investigating consumer complaints (case investigations) (Reactive) or doing planned studies such as surveillance or developing test methods (Proactive). By working with CVM labs to enhance the government's capabilities and improve our ability to can respond to emergencies. Finally, Vet-LIRN supports and encourages professional development of CVM, Vet-LIRN and its network partners to improve response and veterinary science overall.

The Vet-LIRN program also:

- Investigates Consumer Complaint Cases - can be extensive, multi-year effort (JPT)
- Performs Emergency Response Exercises
- Performs Proficiency Testing
- Conducts Method Development (Grants)
- Is a part of the antimicrobial resistance (AMR) initiative for CVM

Aligned Study Indicators of Research Impact

	Preliminary Indicators of Research Impact
Advancing Regulatory Science	• Develop and validate methods to be used by network laboratories. • Conduct investigational testing for analytes that currently do not have FDA validated methods available at ORA laboratories. • Evaluated pet feeds for bacterial pathogens e.g., Listeria/Sal/E.coli; Preformed a collaborative Study to estimate prevalence of Salmonella in the population of dogs and cats across the country (V-CLASP). • Conduct proficiency tests ensuring FDA receives reliable data. • Vet-LIRN leverages FDA Resources to conduct diagnostic method evaluations for matrices ORA labs do not usually test.

Disseminating Scientific Knowledge	• Scientific knowledge out of the Vet-LIRN camp is readily shared: Via many channels: • Information shared via Vet-LIRN online updates, FDA CVM consumer updates, investigation results to OSC, ORA, veterinarians and owners, congressional reports and other briefings, peer reviewed journals, AVMA Webinar on JPTG, monthly calls to facilitate communication with veterinary diagnostic laboratories and with partner agencies, GenomeTrakr and NCBI • Developed a network of laboratories and strategic and Tactical Plans for working with CVM to investigate problems with regulated products.
Informing Regulatory Decision-making	• Vet-LIRN improved CVM's ability to respond to complaints related to FVM-regulated products; increased speed and in-depth evaluations. • Case Investigations identify animal food hazards prompting regulatory testing and result in the recall of products potentially hazardous to humans and animals (e.g. *Salmonella* and *Listeria*). • Provide data for warning notices to the public e.g., related to Jerky Pet Treat Investigation and Raw Pet Food Diets. • Case investigation results provide data for decisions related to FVM-regulated products (OSC, ORA, CBP).
Catalyzing Action	• VetLIRN investigational product testing data resulted in several regulatory field assignments to identify potentially adulterated products. • Vet-LIRN created network of 38 laboratories that interact together, report problems to CVM, conduct investigations. • Multiple industry recalls of contaminated products have occoured due to Vet-LIRN laboratory testing of diagnostic samples and/or open product testing.
Advancing Public Health	• Vet-LIRN is an integral part of the team working to Slow the emergence of resistant bacteria and prevent the spread of resistant infections. • Strengthen National One-Health surveillance efforts to combat resistance. • Advance development and use of rapid diagnostic tests for identification and characterization of resistant bacteria. • Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control, and antibiotic research and development.

IMPACT IN BLOOM

The RIWG conducts an annual retrospective case study review of research initiatives that align with FVM priorities, using framework domains and indicators of research impact, to celebrate strategies put forth to enhance the public health. FVM scientific research studies are submitted by nomination from the Centers and ORA and a select few are highlighted in the OFVM Foods Conference. The studies that remained are deferred for review over the course of the next year or two to allow for the impact of the research to be realized and mature. While the studies within this next section are not yet fully mature, they demonstrate budding impact potential that the team will continue to observe through to maturity and completion.

LEAD AND OTHER HEAVY METALS IN COSMETICS

In December of 2016, the FDA released, "Lead in Cosmetic Lip Products and Externally Applied Cosmetics: Recommended Maximum Level – Guidance for Industry," to document the rationale for recommending the maximum level of lead (Pb) as an impurity present in externally applied lip products as 10 parts per million (ppm). Support for the recommendation results from the outcome of a number of studies – to include this one). While adherence to this FDA issued recommendation is voluntary, new manufactures who wish to enter the market are being encouraged to follow or improve upon these voluntary good manufacturing practices that limit trace amounts of lead as an impurity.

Ahead of conductof this study, often erroneously high levels of lead (Pb) are reported because improper methodology has been used to detect the lead in the lipstick matrix, due to the presence of differing ingredients, including fats, oils, pigments, dyes and minerals. The Agency developed and validated a method for determining lead in lipsticks has begun and will continue to permit FDA to make an independent evaluation of the hazards presented by inclusion of this trace impurity.

Periodically there are reports in the news of dangerous levels of lead (Pb) in lipsticks with the implication that the lipstick, and therefore the lead, is being ingested. Often erroneously high levels of Pb are reported because improper methodology is used to detect the lead in the lipstick matrix. On the other hand, with increased numbers of color manufacturers, there has been an increase in the number of batches of colors rejected for having lead over the specification limits. It may be that colors containing lead are being used in the manufacture of lipstick. FDA developed and validated methods for determining lead in lipsticks will permit FDA to make an independent evaluation of the hazard suggested by media reports.

DETERMINATION OF INORGANIC CHEMICALS RELEASED FROM POLYMER-CLAY NANOCOMPOSITE FOOD PACKAGING

Advancements in nanotechnology have given way to the emergence of the use of Polymer-Clay Nanocomposite (PCNs) as a food packaging option, particularly for potential use in food and beverage packaging, including boil-in bags, microwavable retort pouches, vacuum packs, paperboard cartons, and bottles. PCNs are found in some natural clays as agglomerated bundles of platelets with an individual thickness of about one nanometer and provide enhanced mechanical, thermal and barrier properties. Recently, interest from the food industry has expanded to other polymers such as polyethylene, polypropylene, and ethylene vinyl alcohol (EVOH). The PCNs can be used commercially in both coatings and multilayer structures. There has been some concern that nanoparticles can be released from nanoclay packaging materials when they are physically abused and/or exposed to high cooking temperature, or that they may change the migration properties of the host polymer(s). If nanoparticles and other residual products migrate into foods in direct contact with the materials, they could possibly become a concern to public health. As such, the research the team responsible for this study has undertaken to help the FDA and the industry to decide whether there are safety issues that should be addressed concerning the use of PCN packaging materials for food products. The research undertaken could lead to increased confidence and use of nano-engineered packaging materials for food markets.

Polymer-clay nanocomposites (PCNs) are plastics in which nanoclays are homogenously dispersed. Nanoclays are found in some natural clays as agglomerated bundles of platelets with an individual thickness of about one nanometer. PCNs have had some commercial successes in barrier applications. In particular, the enhanced barrier and mechanical properties of nylon 6 and PET nanocomposites exhibit great potential for use in food and beverage packaging, including boil-in bags, microwavable retort pouches, vacuum packs, paperboard cartons, and bottles. Recently, interest from the food industry has expanded to other polymers such as polyethylene, polypropylene, and ethylene vinyl alcohol (EVOH). The PCNs can be used commercially in both coatings and multilayer structures. When placed in a polymer matrix, nanoclays are hard to be separated or distinguished from the host polymer. However, there has been some concern that nanoparticles can be released from nanoclay packaging materials when they are physically abused and/or exposed to high cooking temperature, or that they may change the migration properties of the host polymer(s). If nanoparticles and other residual products migrate into foods in direct contact with the materials, they could possibly become a concern to public health. Therefore, it is necessary to evaluate the potential migration issue in PCN for food packaging applications. The research the team has undertaken will help the FDA and the industry to decide whether safety issues should be addressed concerning the use of PCN packaging materials for food products. The research could lead to increased confidence and use of nano-engineered packaging materials for food markets.

DEVELOPMENTS IN CYCLOSPORA DETECTION METHODS

Foodborne outbreaks of diarrhea illnesses caused by *Cyclospora cayetanensis* have affected thousands of individuals in several states of the U.S. specially in the last five years. In the fall of 2014, a program was initiated at the CFSAN's Office of Applied Research and Safety Assessment (OARSA) to prioritize the development and validation of laboratory methods for fast and sensitive detection as well as genomics-based approaches to genotype foodborne parasites. As the first major outcome, a method to recover, detect and characterize *C. cayetanensis* in fresh produce underwent multilaboratory validation for use on five types of produce matrices and is available in the FDA's Bacteriological Analytical Manual (BAM) under a chapter entitled "BAM 19b: Molecular Detection of *Cyclospora cayetanensis* in Fresh Produce Using Real-Time PCR". The method can also be used to detect *C. cayetanensis* in prepared dishes and is being implemented in all regional ORA laboratories to be used in assignments to ascertain the prevalence of *C. cayetanensis* in produce and assist with outbreak investigations. This method will be the backbone of an international standard to detect *C. cayetanensis* in

foods for the International Organization for Standardization (ISO). Since 2016, this method is being used to support the IMPORT ALERT #28-11, "Detention Without Physical Examination of Aromatic Herbs Due to the Presence of *CYCLOSPORA CAYETANENSIS*". Because agricultural water may play a role in contamination of produce with this parasite, this program also prioritized the development of a method for sensitive and specific detection of *C. cayetanensis* in such samples. Multiple laboratory protocols and bioinformatics analysis methods were developed and tested allowing the sequencing of the whole genome of *C. cayetanensis* including its organellar genomes. The high-resolution molecular data accumulated from the genome sequencing research will be the basis for molecular epidemiology methods to type *C. cayetanensis* in clinical, food and environmental samples. A *Cyclospora cayetanensis* GenomeTrakr database was created as an umbrella BioProject within NCBI to consolidate all the genome data being generated by the FDA, and other HHS sister agencies as well as to network collaborators worldwide. The methods and approaches developed and validated under this program will be used to track the sources of food contamination providing support to epidemiological investigations and regulatory actions to strengthen food safety.

Because agricultural water may play a role in the contamination of produce with this parasite, this program also prioritized the development of a method for sensitive and specific detection of *C. cayetanensis* in such samples. Multiple laboratory protocols and bioinformatics analysis methods were developed and tested allowing the sequencing of the whole genome of *C. cayetanensis* including its organellar genomes. The high-resolution molecular data accumulated from the genome sequencing research will be the basis for molecular epidemiology methods to type C. cayetanensis in clinical, food and environmental samples.

SUCCESS STORY PRINCIPAL INVESTIGATOR AND IMPACT IN BLOOM POINTS OF CONTACT

Case Study	Point of Contact
Quantification of Plant Sterols/Stanols in Foods and Dietary Supplements Containing Added Phytosterols: A Multi-lab Validation	Cynthia Srigley; Cynthua.Srigley@fda.hhs.gov
Development of a Multiresidue Method for the Determination of Hormones in Bovine Muscle Tissues	Pak-Sin Chu; Pak.Chu@fda.hhs.gov
THE Vet-LIRN Program	Renate Reimschuessel; Renate.Reimschuessel@fda.hhs.gov
Developments in Cyclospora Detection Methods	Alexandre DaSilva,;Alexandre.DaSilva@fda.hhs.gov
Lead and Other Heavy Metals in Cosmetics (in CARTS - Development and Validation of Methods to Determine Lead in Lipsticks)	Nancy Hepp; Nancy.Hepp@fda.hhs.gov
Determination of Inorganic Chemicals Released from Polymer-clay Nanocomposite Food Packaging	Tim Duncan; Timothy.Duncan@fda.hhs.gov

WHERE TO GO FOR MORE INFORMATION

RESEARCH IMPACT

BAM Online, http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm114664.htm

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