
Emerging Biotechnologies to Promote Safety, Enable Defense and Discourage Fraud

Q&A

MODERATOR: FRANK BUSTA

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Frank Busta: Our three panelists are here and it's time for your questions.

Kim Nill (US Soybean Export Council): Dr. Moore, certain countries and certain buyers of organic commodities might consider so-called GMOs as adulterants of non-GMO commodities. Considering the detection methods, it seems to me to be hopeless because virtually all of the relevant genes in biotech products come from soil-dwelling bacteria, *Bt*¹ for instance. These commodities are allowed as much as 2% of what is called foreign material. That 2% could be entirely top soil, so you would have false positives triggered by bacteria that just happened to be present. Getting anything approaching a scientific determination of what is present strikes me as hopeless. Am I missing something, or is there a way around this?

Jeffrey Moore: Your question speaks to a real challenge in that the more specific and the more selective the method, the greater is the chance of false classification, because you simply have more and more information making it more difficult to determine whether or not something is authentic. ELISA²s, which are used widely do have this very real issue of false positives and false classifications. On your question about GMOs, I don't take a stance on that. At USP³, standards are not being developed to differentiate GMOs from non-GMOs. I don't see us doing that any time in the near future, if that's what you were getting at.

Tracy Sides (University of Minnesota): Yesterday, we heard that, at the beginning of their *E. coli* outbreak, Germany turned to a lab in China rather than to a lab here in the United States, which was described as a negative reflection on public funding support. I'm curious, Dr. Besser, regarding your perspective on that occurrence.

¹*Bacillus thuringiensis*.

²Enzyme-linked immunosorbent assay.

³US Pharmacopeia.

John Besser: I was a little mystified as to why China was the first laboratory to sequence that organism. I really don't know the story. Yes, it's true that our infrastructure is under-funded to keep up with these technologies. When the cholera outbreak occurred in Haiti some months ago, we actually did have that whole thing sequenced within a few days. We threw resources that we didn't have at it, so it's possible to do. To answer your question: yes, there is an issue but I don't know why that occurred.

Joseph Msanne (University of Nebraska): Dr. Moore, are food preservatives considered adulterants?

Moore: There are many cases where they can be, especially where they are not allowed for use in food products. Shelf-life extension adds value to it, so it may be considered EMA⁴ or food fraud.

Shaun Kennedy: There are examples of that being done in which the contaminant poses public-health problems. There was a case in China where a company added formaldehyde in order to extend the shelf life of tofu.

Hongshun Yang (University of Minnesota): A question for Dr. Besser...[inaudible]

Besser: The power of PulseNet is that everybody uses the same protocol and there is a certification process for laboratories to become part of PulseNet, to use the brand name. So, yes, the results are mostly comparable throughout the world. Unfortunately in the 2011 German outbreak, although we had added a new non-O1576 protocol—details of which you really don't need to know—the Germans hadn't yet adopted it. So, we actually couldn't directly compare the patterns that they were getting with ours. Every attempt is made to have uniformity throughout the world so that we can compare—eventually instantaneously—one country to another country. The problem with PulseNet International mostly is that the surveillance systems in different countries vary tremendously, and, in many countries, surveillance as we know it barely exists. So while countries may develop this very robust infrastructure at the national level, they may have very little to work with; doctors aren't ordering tests, laboratories aren't identifying bacteria, samples aren't being sent to health departments. In order to make this work in much of the world, we have to address the underlying public-health infrastructure, which of course is a much bigger task. But we actually are doing that through a program called the Global Foodborne Infections Network, or GFN, where we are holding epidemiology and laboratory-training classes throughout the world. Interestingly, the microbiologists argue a lot about methods, but it actually doesn't matter. You hit upon the really important point that everybody should do the same thing, whatever it is. I wish I could clobber the Europeans over their heads so that they get that one point. It's important that we all do the same thing, that we speak a common language.

⁴Economically motivated adulteration.

Jacqueline Fletcher (Oklahoma State University): I have a question about the response of systems that are the same or different when an intentional contamination might be involved. Does it change who responds, who takes control and how initial decisions are made? And maybe you could put it in the context of the German outbreak. I know that people have considered the possibility that that was intentional—there are odd things about it—but, as far as I know, there's no evidence for that.

Besser: When clusters of disease occur, we don't know whether they are foodborne if we don't know why they are occurring. We don't know whether they are intentional or natural occurring. In fact, we don't know anything other than that a cluster of disease is occurring. So the initial process is an epidemiological one, attempting to answer some of those basic questions. If there's any hint of intent, then Homeland Security and other organizations would quickly come into it and we'd have phone conferences with the Departments of Defense and Homeland Security very early on because of the unique nature of this, and they would ask us directly what evidence we have that it wasn't intentional and what level of concern should they have. And we would share with them all of the available epidemiologic data to try to assess, to triage the level of concern that we have an intentional event. And, in this circumstance, while it couldn't be ruled out, there was no specific intelligence or any specific microbiological data to point towards intentional contamination. But this has to be asked every time. We are the gatekeepers because we are investigating the clusters and the threshold is pretty low. If there is any concern we get the intelligence agencies involved very quickly.

Kennedy: In the United States specifically, when it becomes a probable intentional event then the FBI becomes the lead agency and Homeland Security becomes the coordinating agency. Three years ago, we had an exercise on food defense that involved the G8 countries and, although most of them don't have an equivalent to Homeland Security, the same basic approach applied; as soon as it becomes potentially intentional the federal law-enforcement agency takes the lead, which introduces challenges in terms of potential differences in investigative protocols between public health and law enforcement. You may end up compromising the public-health investigation because you are trying to make sure you have an appropriate law-enforcement investigation.

Busta: And, at that G8 event, the German representatives said they had it all down cold.

Jacqueline Fletcher (Oklahoma State University): 99.99% of outbreaks are unintentional. What is the status of research in preparation for types of work that had to go on, say, after the anthrax attack to pin down the source—in other words, very detailed, strain-discriminatory testing, markers and so on?

Besser: The microbiological aspects are relatively easy to control. We can do whole-genome sequencing for about \$100 now. Unfortunately, unlike in human DNA sequencing for

forensic purposes, as used with OJ Simpson and the bloody glove, the system that we are operating in is a lot more complicated. It is sufficiently complex that microbiological data alone often don't tell the story. The natural variation in the bacteria complicates this whole concept of microbial forensics. Even with anthrax. Anthrax was a perfect case because it's something that's at an extremely low prevalence in the population and its presence in a human case is indicative of an extraordinary event. When you are talking about things that are common, like chicken pox or *E. coli*, it gets much more complicated. The germs are constantly changing on their own, and we actually pick markers that are variable. We pick them because they are variable. In the Haiti outbreak, for instance, we sequenced sixteen strains; differences occur as it's passed from person to person so they are constantly changing. While it's an emerging science and we can tell a lot from the germs, it has to be a multi-systems approach to get at these issues. The science has progressed, but we are running up against a wall; microbiology can't tell us everything.

Busta: How would you go about trying to detect whether it was a laboratory-directed change in the organism compared to one that's natural?

Besser: We haven't encountered that yet, fortunately, but we can look at the sequence level and there are certain natural insertion sites for genes that are well known in the molecular biology world. So one can look for insertions of chunks of DNA that might not be appropriate. This actually did occur with smallpox, when interleukin-2 was introduced in Britain, I believe, in the 1990s. This was not a bioterrorism event, it was just an experiment. I am not a molecular biologist, but I know that there are ways of looking for these large insertions and deletions of genes.

Francisco Diez-Gonzalez (University of Minnesota): It's been over seven years since then-US Secretary of Health Tommy Thompson said, "For the life of me, I can't understand why terrorists haven't attacked our food supply." What are we doing right, that this hasn't happened?

Busta: Alright, Shaun?

Kennedy: Part of it is, they actually have been plotting to try and do something intentionally to the food system and have been caught before they did it. Law enforcement has actually gotten lucky a few times. And part of it was touched on yesterday, about the psychology and sociology of terrorists—what their motivation is—and right now they are satisfying their membership motivation by blowing themselves up in the Middle East. Until we are out of Iraq and Afghanistan they are going to be focused there more than they will be focused here because their primary goal is to get us out. And attacking us here, as they learned from 9/11, doesn't get us out. It brings us in.