CDC 24/7: What's Really in a Cigarette?

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In the challenge to regulate tobacco products, the FDA has a formidable weapon—CDC's Tobacco Laboratory.

Housed at CDC's Chamblee campus, the laboratory is part of NCEH's Division of Laboratory Sciences and provides the National Health and Nutrition Examination Survey (NHANES) data that tracks exposure to constituents of tobacco smoke in the US population.

An important measurement from the Tobacco Lab that tracks exposure to tobacco smoke is serum cotinine. Cotinine is the main breakdown product of nicotine in the body and persists in the body longer than nicotine. Serum cotinine data from the Tobacco Lab documenting secondhand smoke exposure in almost 90 percent of the US population was highly influential in promoting the banning of smoking in public places, including work places and restaurants in the mid-1990s. The policy's enforcement nationwide has resulted in a consistent drop in exposure, say CDC scientists.

"Between 1988 and 2001, there was a 76 percent drop in cotinine levels among nonsmokers," says Connie Sosnoff, MS, a research chemist in the Tobacco Exposure Biomarker Lab, which measures nicotine exposure in people's urine, serum, plasma and saliva.

New Legislation Brings Sharper FDA Regulatory Role

With the passage of the Family Smoking Prevention and Tobacco Control Act of 2009, the FDA has regulatory authority over tobacco products for the first time in history. The FDA is positioned to evaluate tobacco products, which many hope will lead to limitations on the harmful chemicals that can be in these products. Soon after the legislation became law, FDA, the Tobacco Lab, and CDC's Office on Smoking and Health signed an interagency agreement to work together to ensure there is a sound science base to any future regulations of tobacco products.

CDC's 24/7 mission—saving lives and protecting people—makes a difference. "Our lab will document exposure to the addictive and toxic substances in tobacco products and the effects of regulation on reducing those exposures," says James Pirkle, MD, PhD, director of the division, who notes that the FDA's regulation of tobacco products is dependent on very good laboratory data.

"Our biggest priority this year is to meet the FDA need to develop profiles of the levels of toxic and addictive substances in the 50 top US brands," he adds.

David Ashley, PhD, an FDA scientist who helped establish the Tobacco Laboratory in 1994 when he worked for CDC, now serves as director of

A CDC scientist examines physical properties and tobacco blend, using a combination of techniques including microscopy. Provided *by Division of Laboratory Sciences*

The CDC Tobacco Laboratory uses automated smoking machines for cigarette testing in combination with advanced analytical techniques, such as mass spectrometry. *Provided by Division of Laboratory Sciences*

David Ashley (left) leads a Tobacco Lab tour for the CDC director and FDA representatives in 2009. Jim Pirkle Tom Frieden, Peggy Hamburg and Joshua Sharfstein participate.

FDA's Office of Science in the Center for Tobacco Products. The FDA office was created in 2009 as a result of the Family Smoking Prevention and Tobacco Control Act. He says while FDA works with many entities, from academic institutions to NIH, its partnership with CDC is particularly strategic.

Some of the tobacco products CDC has analyzed, on display inside a glass case. *Photo by Provided by Division of Laboratory Sciences*

"As an HHS partner, we are brother and sister, not just neighbors," says Ashley. "We depend very heavily on the laboratory at CDC since the foundation of everything we do is based on science. The folks of CDC are providing a tremendous amount of information for us that will really make a difference long term in ensuring the regulations we write are as effective as possible," he says.

In addition to the CDC lab's helping to evaluate methods and develop new analytical methods for measuring what's in tobacco products, CDC also will help train FDA's compliance laboratory based in Atlanta on methods for analysis of tobacco products.

According to Ashley, the FDA has taken several actions since it was granted the authority to regulate tobacco products. The agency has issued guidance on demonstrating substantial equivalence of tobacco products, new tobacco product applications, and modified-risk tobacco products. The most public move the agency has made is in issuing new graphic health warnings which, if upheld in US courts, will be visible on every cigarette package. In addition, FDA has put out a list of harmful and potentially harmful constituents that the industry must report to the government, and has required the industry to list all ingredients in its tobacco products.

No Single 'Smoking Gun' with Tobacco

HHS long has had the tobacco industry's so-called "599 list," but the ingredients laid out are deliberately vague, including descriptors like "botanical extracts" – a grouping that isn't one compound, but could be a thousand compounds. For this reason, CDC and the FDA aren't relying just on industry disclosure. The industry has rationalized the use of many additives as being "generally regarded as safe" for food.

A close up of the smoking machine. *Provided by Division of Laboratory Sciences*

Observes Cliff Watson, PhD, lead research chemist at the Lab: "There is no smoking gun in cigarettes and tobacco; there are not just one or two bad actors; there are 50, 60 or 100 acting in concert."

He explains that inhalation is a much different route of exposure than eating a substance since the digestive system is designed to take some pretty nasty hits and recover.

"You have a couple of ways your body can detoxify," he says. "The bottom line is when you smoke tobacco, the smoke goes into your lungs and straight into your bloodstream. Unlike products that we eat, there's no first pass to detoxification. That's where the potential real harm comes from."

The nation's Surgeon General Regina Benjamin, MD (center) recently toured CDC's Tobacco Laboratory, located on the Chamblee campus in the Division of Laboratory Sciences, NCEH.

Even though smoking is the leading preventable cause of lung cancer, prior to the passage of the law, tobacco products in the United States were completely unregulated.

Watson began working in the tobacco product area 14 years ago, admittedly coming to this work "late," given that CDC started work in tobacco analysis beginning in the late 80s and early 90s.

"Our first smoking machine was a 50-milliliter syringe," says Ashley, who along with other chemists attached a cigarette to the end of a syringe, which would simulate taking a puff of smoke when they pulled up the syringe. "We injected the smoke into a bag, which we could take

into the laboratory and analyze it." Ashley says that back then the Chamblee campus had smoking booths resembling bus stops. He and his colleagues would go into those booths and simulate smoking cigarettes using this syringe.

"We were reading a lot and trying to find out what we could. At the time, most of the work on product was being done by industry and they published very little of that work. It was very interesting and challenging and was brand new for us. There were very few people we could consult with and ask for help. We tried to keep it very scientific. Everything we did was based on the science to establish our reputation – that we could look at smoke and make measurements," he says.

The lab has come a long way since those humble beginnings. In the last two years, the CDC Tobacco Lab has doubled in size, since the Division of Laboratory Science developed the science base and the investigative methods to measure tobacco compounds. Watson's team is using the latest technological tools to determine what compounds are in tobacco products and in what concentrations.

"We look at the whole exposure gamut – what's in the product, what's in the smoke, and ultimately, what gets into people," he says.

Lab Tour Shows Growth in Smokeless Products

CDC Connects recently toured the Tobacco Lab, during which Watson showed a glass case filled with different tobacco products from around the world. The cigarettes, cigars, chewing tobacco and other products showed changes in labeling, with some packages carrying the "light" or "ultra light" wording now banned because the wording was determined to mislead consumers.

New smokeless tobacco products were the newest additions to the exhibit. Formerly a very small segment of the industry, smokeless products are becoming more important, as evidenced by major tobacco firms acquiring smaller players in the space. Many smokeless tobacco products are marketed as a way to circumvent indoor air restrictions and to make these products more acceptable to the general population.

"They are called bridge products – you can use these products very discreetly and they'll bridge you to your next cigarette," says Watson, showing a range of samples from tiny nicotine pieces resembling Tic Tac® candies, to tobacco powder that can dissolve in one's mouth, leaving no residue and no need to spit.

The FDA today has regulatory authority over cigarettes, smokeless and roll-your-own tobacco, but the agency has expressed its intention to expand regulatory authority to cover other tobacco products not currently regulated, says Ashley.

Influencing tobacco product standards is another area of focus for the FDA. "Product standards provide us a very broad range of ways we can go in and impact the products themselves. We can set regulations related to the products," says Ashley, adding that one potential area mentioned specifically in the Tobacco Control Act is changing the levels of nicotine in tobacco products.

Robotic-Run Smoking Machines Analyze Lit Cigarettes

Further into the lab, chemists and other scientists in lab coats wear eye protection as they analyze the chemical compounds from captured smoke. The lab operates a number of totally enclosed smoking machines. They range in size from eight-port and 20-port chambers. A robotic arm lines up cigarettes into ports and lights them one by one. Jets of smoke emit from the cigarettes as if invisible smokers are inhaling. Once the cigarette is spent, the robotic arm cuts and discards the spent cigarette butt. Throughout the smoking process, the smoke is collected on filter pads and in gas sampling bags and transported to other equipment, primarily mass spectrometers, for further analysis.

"We look at what's native to the tobacco, what's added by the manufacturer, what happens when you burn it. We do some work in the topography of how people smoke, based on product design," says Watson.

From there, the Tobacco Exposure Biomarker Lab takes over, evaluating what is occurring in smokers

and non-smokers who are exposed.

“We provide a picture of what is in the bodies of smokers right now, and then as the FDA regulates tobacco, we are going to take pictures along the way in smokers to see if these toxic elements are diminished based on FDA regulation,” says Sosnoff, who joined the lab in 1992 when there were only five staff members. Since that time, “we’ve tripled our laboratory staff and we've added many new biomarker measures.”

One of the new biomarkers is NNAL. NNAL is a metabolite of NNK which is a tobacco-specific nitrosamine and a lung carcinogen. NNAL has only been analyzed for the last four years in the NHANES population. The assay is very complicated and the compound is present in very low concentrations in urine. “The detection approach relies on tandem mass spectrometry which is very sensitive and specific and has a high throughput. The beauty of this technology is it can be automated. You can queue up samples in the evening and let it run all night.” According to Sosnoff, the last two NHANES cycles show a drop in NNK exposure.

CDC to Increase Lab Capacity, Including Investing in Automation

Looking ahead, Pirkle says it’s critical that the tobacco-specific laboratory capability remains at CDC, citing two reasons – one, it would be technically difficult to replicate elsewhere, and two, CDC has amassed a very specialized staff to do this type of work.

“We have acquired over time a broad group of experts who collectively are the strongest analytical group anywhere for making these measurements on tobacco products, smoke and in people,” he says.

Watson expresses optimism for the groundwork being laid. CDC is looking to increase the level of automation in the lab as well as the headcount, so it has the capacity to handle the volume of tobacco samples that the FDA will need analyzed as it looks at new regulations.

“We’re developing the right data now that the FDA can use to issue meaningful product guidelines. The public health community is very conscious that the regulations must have a scientific basis and the impact of the regulation must be monitored to see if the regulations are having the desired effect,” says Watson.

As for CDC staff, Watson hopes that the presence of the Tobacco Lab serves to raise awareness on the dangers of tobacco use.

“If we have any tobacco users in CDC, we want to educate them that there is no such thing as a safe product,” he says. “Hopefully, they can quit or get into programs to help them quit. It’s a very addictive substance.”

For more, visit:
The nation’s Surgeon General Regina Benjamin visit
Tips from Former Smokers Campaign

Find tools you can use, from slides and talking points to help you in presentations as you incorporate our 24/7 message into all your talks.

And visit the Director’s Corner each week for the latest 24/7 fact. Learn more about CDC’s 24/7 mission.

This ***Inside Story*** by Anne Wainscott-Sargent.

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