

NIH at Forefront of New Clinical Trials Push

Academic researchers encouraged to partner with NIH to move new drug candidates to the next step.

BY MARK S. LESNEY

FROM THE ANNUAL MEETING OF
THE AMERICAN SOCIETY OF HUMAN GENETICS

WASHINGTON – Breakthroughs in human genetics combined with funding from the Affordable Care Act have poised the National Institutes of Health to make real progress in the areas of orphan human diseases, according to NIH Director Francis S. Collins.

Speaking with enthusiasm to those he addressed as his “peeps” at the annual meeting of the American Society of Human Genetics, Dr. Collins shared his excitement at the state of human genetics in the post-genomic world, in large part driven by technology that has significantly lowered the cost of DNA sequencing, in turn speeding genetic research tremendously.

This, combined with new ACA funding, has enabled NIH to fund and pursue translational research, moving laboratory results toward and into clinical trials, something that is a new way of thinking for the agency, Dr. Collins said.

Rather than relying on pharmaceutical and biotechnology companies to take charge of the translational research, Dr. Collins encouraged academic researchers to consider partnering with NIH, at least for those orphan disease conditions in which the federal government would not be seen as being in competition with private enterprise.

“There is a serious crisis underway in the way in

which this pipeline for drug discovery has been floundering. ... Pharma has been investing a larger and larger amount of money – between \$40 and \$50 billion dollars a year – and yet in spite of that, FDA approvals of new molecular entities, that is genuinely new drug therapeutics, not ‘me-toos,’ have been dropping steadily over the last 15 years,” Dr. Collins said.

The reasons for this are complex, he said, but a big part of the problem involves coming up with appropriate targets and targeting compounds. He said this is an area in which NIH is and can be very much involved.

NIH now encourages academic researchers to take their targets to the assay stage and beyond, providing high-throughput screening (HTS) assistance from the NIH Chemical Genomics Center. Subsequent medicinal chemistry assistance is also available to help to modify HTS hits to enable compounds to become more drug-like and to match current ADME (absorption, distribution, metabolism, and excretion) criteria.

With NIH assistance, more than 150 lead compounds have reached this stage over the last 4-5 years, more than half of which are “poised to go to the next step” of pre-clinical trials in animals, or the “Valley of Death,” according to Dr. Collins, “because this is where projects often go to die.”

NIH is now able to assist in this high-risk area through the Therapeutics for Rare and Neglected Diseases (TRND) program in its Office of Rare Diseases Research. The TRND was funded at \$24 million in fiscal year 2009.



Despite annual investments of up to \$50 billion by the drug industry, FDA approvals of new entities have dropped steadily.

DR. COLLINS

NIH also is positioned to assist researchers in early phase human trials of orphan diseases through its 240-bed Clinical Center, Dr. Collins said.

“And we have 50 and soon we will have 60 Clinical and Translational Science Awards scattered all across the country which will also be set up to conduct these sorts of trials for new molecular entities,” Dr. Collins added.

This new direction in research funding has involved unprecedented cooperation with the Food and Drug Administration, Dr. Collins said, with an NIH-FDA leadership council formed to ensure that new drug candidates are most safely and efficiently moved into the clinical trials framework in ways that would best enable FDA analysis and validation, particularly for rare diseases.

Dr. Collins was particularly excited about five instances in which NIH is using this new model of helping “de-risk” the drug development process for orphan or neglected diseases through TRND. These include four rare diseases (Niemann-Pick disease type C, hereditary inclusion body myopathy, sickle cell disease, and chronic lymphocytic leukemia) and one neglected disease (schistosomiasis).

If and when these compounds and those for other rare diseases become ready for marketing and production, NIH would then work with private companies to achieve licensing agreement to enable their manufacture and sale, according to Dr. Collins.

Dr. Collins reported having no financial conflicts of interest with regard to his presentation. ■

Alcohol Tax Boost Touted to Yield Public Health Benefits

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE
AMERICAN PUBLIC HEALTH ASSOCIATION

DENVER – Doubling the currently low alcohol tax would result in roughly a 35% reduction in direct alcohol-related mortality as well as substantial benefits across a range of other important public health outcomes, a meta-analysis has shown.

“We have a lot of literature. This is probably the most studied preventive health policy issue. The magnitude of the observed effects is larger and more consistent than for most other preventive efforts that’ve been studied,” Alexander C. Wagenaar, Ph.D., said at the meeting.

He presented a meta-analysis based on what he described as “an exhaustive search” of the past 50 years of published studies on the effects of alcohol tax pricing policies on a whole range of public health outcomes.

In summary, a 10% increase in the alcohol tax and a commensurate price increase would result in an across-the-board 5% reduction in drinking across all groups: underage teens as well as adults, moderate as well as heavy drinkers.



The meta-analysis of 50 studies showed that doubling the alcohol tax would be associated on average with a 35% reduction in deaths due to cirrhosis, some cancers, and other directly alcohol-related causes; an 11% drop in traffic crash morbidity and mortality; a 6% decrease in sexually transmitted infections; a 2% reduction in violence;

A 10% tax increase and a price increase would result in a 5% reduction in drinking across all groups.

DR. WAGENAAR

University of Florida, Gainesville.

“This is a policy that applies at the population level. It’s not just for the high-risk group, it’s not only for the people that get into treatment. When a tax change is implemented, it changes the environment slightly across the entire population such that there’s a reduction in drinking, and that effect ripples across these whole sets of alcohol-related outcomes,” explained the researcher, whose prior health policy studies have been credited as playing a key role in establishing the uniform nationwide drinking age of 21.

Suicide was the only outcome the in-

vestigators studied that didn’t show a significant decrease in response to an increased tax on alcohol. Most of the 11 relevant studies have been conducted by only two research groups.

“There’s not enough evidence yet to determine conclusively whether change in alcohol taxes influences suicide rates,” Dr. Wagenaar said.

He pointed out several practical advantages to raising the alcohol tax, beyond the striking public health benefits.

An alcohol tax increase would generate additional revenues that could be used to fund other public health objectives or to bolster the general fund. No costly new bureaucratic infrastructure is required to implement an alcohol tax increase; the tax structures are already present. And alcohol tax rates are now at historic lows because they’re volume-based and aren’t adjusted for inflation.

“That’s how we’ve gotten into this situation where the tax rates now are only a fraction of what they were in the 1950s, ’60s, and ’70s. If we were to simply return the tax rates in most jurisdictions to the rates that were in place in the ’60s and ’70s, we would see the kinds of effects that we’re seeing in the meta-analysis, because in many areas that would involve a doubling of the tax rates,” Dr. Wagenaar said.

In response to an audience question, he said the available evidence indicates

there is no threshold effect for the relationship between alcohol tax increases and public health benefits. In other words, if the alcohol tax is increased by, say, one-quarter, public health benefits will accrue, albeit not with the same large effect sizes as with a doubling of the tax.

Dr. Wagenaar’s study was funded by the Robert Wood Johnson Foundation. He said he has no relevant financial conflicts of interest. ■



A change in the alcohol tax has a ripple effect “at the population level.”