Association for Molecular Pathology
Promoting Clinical Practice, Basic Research, and Education in Molecular Pathology
9650 Rockville Pike, Bethesda, Maryland 20814
Tel: 301-634-7939 • Fax: 301-634-7990 • Email: amp@asip.org • *www.amp.org*

Comments by Jan A. Nowak, M.D., Ph.D.
On behalf of
The Association for Molecular Pathology
The Clinical Laboratory Improvement Advisory Committee
September 2-3, 2009

Dear Members of the Clinical Laboratory Improvement Advisory Committee:

I am Jan Nowak, President of the Association for Molecular Pathology. AMP is an international medical professional association representing approximately 1,500 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. The vast majority of our members work in CLIA certified, CAP accredited, clinical laboratories.

In light of your agenda's focus on ensuring laboratory testing quality during a public health emergency, I would like to share with you some of my experiences and observations of how clinical molecular diagnostics laboratories responded to the pandemic H1N1 flu outbreak last spring.

As background, you should know that a significant number of clinical laboratories routinely perform molecular testing for influenza. In the latest CAP Proficiency Test Survey for respiratory viruses, 104 laboratories participated in the influenza virus challenge, and achieved a consensus response of 95%. In 2008 the consensus response was 100%. Approximately one third of the participating laboratories reported using user developed assays; the remainder used commercially available assays. This data highlights the effectiveness of current CLIA regulations for molecular testing, many of which are laboratory developed, and for influenza testing in particular. I think you will find that the quality of influenza testing during the H1N1 outbreak meets this same high standard.

Last April, when the first reports of the novel H1N1 influenza strain began to appear, these laboratories were confronted with the task of providing timely, useful information to their clinicians about this new infectious agent. Early in week one of the outbreak, the molecular laboratories in the Chicago area participated in a conference call with the Illinois Department of Public Health to exchange information about tests in use, testing capacity, confirmatory capabilities, etc. Within a week the community labs had sufficient information to know that available assays for influenza A were capable of detecting the novel H1N1 strain, and furthermore, that some assays were capable of specifically identifying the novel H1N1 subtype. This knowledge greatly reduced the number of specimens that needed to be confirmed by IDPH. By the end of the first week of the H1N1 episode, our own laboratory had identified 39 cases of probable H1N1 infection,

only a fraction of which had been corroborated by our state public health laboratory, and confirmed only sometime after day 8. The CDC tally for all of Illinois at the end that week was still only 3 cases confirmed, a number widely reported in the media, misinforming the public and the medical community of the true nature of the pandemic. By the end of week two of the outbreak, many labs had sufficient data from IDPH to validate their assays, and were asked to limit their submissions for IDPH confirmation. After four weeks, more cases of H1N1 had been diagnosed in community molecular diagnostic laboratories (790 cases) than by IDPH (698 cases).

An informal survey of AMP member laboratories during the first week of the H1N1 episode showed that 93% of the 43 respondents had a molecular assay that could detect and distinguish Influenza Type A from Type B. Those laboratories had an aggregate test capacity of 3,000 to 4,000 specimens/day, and could expand their capacity to as much as 12,000 specimens/day within 30 days if needed. Thirty-six percent of the laboratories reported having the capability of distinguishing the novel H1N1 strain from seasonal H1 strains. During week one of the outbreak, those laboratories had an aggregate test capacity approaching 2,500 specimens/day, with a potential of nearly 8,000 specimens/day within 30 days.

It is important, too, to note that reports from these laboratories are largely available within 24 hours of specimen collection, a degree of timeliness not likely to be matched by any public health laboratory. There can be no argument that accurate, timely data are crucial for making public health decisions in the first hours and days of an emerging pandemic. For clinical decisions, for rational choice of anti-viral therapy, timeliness is essential.

What elements were in place that made this rapid, effective laboratory response possible? We can point to several key factors without which this kind of response could not have occurred.

First, we need to acknowledge that there exists in this country a large network of well developed molecular diagnostics laboratories, operating under CLIA certification and predominantly CAP accredited. Some of these are located in academic centers, but others are very much in the community hospital setting. Characteristically, these labs are staffed by directors and personnel trained in molecular diagnostics, with expertise in the development and validation of these clinical tests. This rich resource is generally undervalued, unappreciated, and, as evidenced in this most recent public health emergency, underutilized.

Secondly, the ability of clinical laboratories to respond as they did was very much tied to their ability to develop and validate their own assays, adhering to CLIA and CAP guidelines. This ability to develop new analytical procedures in response to clinical need is deeply rooted in the tradition of clinical pathology. The AMP survey respondents employed more than 5 different commercial assays (ASR and IVD) in their laboratories, and 18% had non-commercial LDT's in use. FDA cleared or not, none of these existing assays had been approved for the detection of the novel virus, and all required adaptation and validation by the individual laboratory.

In a public health emergency test validation, as always, needs to be rigorous and thorough, but it need not be slow. Indeed, the vast majority of molecular diagnostic tests for infectious agents originate as clinical LDT's in response to clinical need, and it is exactly that facility afforded the clinical laboratory that is called for during a public health emergency. Leveraging that capability for the benefit of the public's health, however, does call for forethought and planning.

Finally, communication and collaboration with local public health laboratories (PHL) are essential. The primary functions of the community molecular diagnostics laboratory and the PHL are not the same. The former is focused on rapid diagnosis for patient care, and in a pandemic, for effective infection control and possible allocation of limited resources. The PHL necessarily takes a broader view to understand the epidemiology of the pandemic with an eye to formulating public policy. Both activities are necessary, but they are not independent. Understanding and coordinating their different roles not only enhances their respective values, but results in an efficiency that cannot be achieved otherwise.

In the next pandemic, in the next H1N1 wave to visit this country, it is reasonable to expect that most infected individuals will be diagnosed with a test performed in a community molecular diagnostics laboratory. Appropriate treatment decisions, effective infection control measures, and prudent use of anti-viral agents all demand accurate and timely diagnoses, and will drive the further implementation of molecular assays. AMP believes that hospital and community molecular diagnostics laboratories offer an unprecedented resource to our public health pandemic planning efforts, and suggest that they be an integral part of future strategic planning, working in concert with public health laboratories and the CDC.

In the recent H1N1 outbreak, I believe the quality of laboratory testing has been outstanding, as has been the response of molecular diagnostics laboratories to this public health emergency. AMP encourages the CLIAC to recognize the quality of testing performed during this period and note the remarkable resource that exists in clinical molecular diagnostics laboratories. Thank you for your attention.