

29 June 2010

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

Should you wish to be removed from this Pandemic Influenza Edition address group, just send an email to one of the people listed at the bottom of this message. This will not affect your continued receipt of the CB Daily.

Chem-Bio News – Pandemic Influenza Edition #118

1. TAMIFLU AND RELENZA EMERGENCY USE AUTHORIZATION DISPOSITION

LETTERS AND QUESTION AND ANSWER ATTACHMENTS: *“On June 21, 2010, the U.S. Food and Drug Administration (FDA) notified the Centers for Disease Control and Prevention (CDC) that these EUAs will terminate when the Public Health Emergency determination for 2009 H1N1 Influenza expires on June 23, 2010. Therefore, after June 23, 2010, the EUAs authorizing the unapproved uses of Tamiflu and Relenza will no longer be in effect.”*

2. WHO SEES POCKETS OF PANDEMIC FLU AND MORE H3N2: *“Pandemic flu activity remained low in most parts of the world, though some areas such as Caribbean countries continued to see active transmission, with increased activity reported in a few areas, including Colombia and parts of India, the World Health Organization (WHO) said today. After rising throughout winter and spring, levels of influenza B transmission throughout the world are decreasing, while influenza A (H3N2) viruses are increasing in some areas such as East Africa and South America, according to the WHO.”*

3. A NOVEL ANTI-INFLUENZA COPPER OXIDE CONTAINING RESPIRATORY FACE MASK: *“Copper oxide displays potent antiviral properties. A platform technology has been developed that permanently introduces copper oxide into polymeric materials, conferring them with potent biocidal properties.”*

4. SIMULTANEOUS TYPING AND HA/NA SUBTYPING OF INFLUENZA A AND B VIRUSES INCLUDING THE PANDEMIC INFLUENZA A/H1N1 2009 BY MULTIPLEX REAL-TIME RT-PCR: *“The analytical sensitivity is 10-10(4) copies/reaction. The coefficients of variation of inter-assay and intra-assay are 0.04-0.45% and 0.08-0.97%, respectively. The new multiplex rRT-PCR assay is more sensitive in subtyping seasonal influenza viruses than the conventional PCR techniques.”*

5. EVALUATION OF QUICKVUE INFLUENZA A PLUS B RAPID TEST FOR DETECTION OF PANDEMIC INFLUENZA A/H1N1 2009: *“There was a significant inverse association between Ct values and QV sensitivity for pandemic influenza A/H1N1.”*

6. DEVELOPMENT AND SUSTAINABLE MANUFACTURING OF ADJUVANTED PANDEMIC INFLUENZA VACCINES IN DEVELOPING COUNTRIES: *“The synopsis for*

this grant opportunity is detailed below, following this paragraph. This synopsis contains all of the updates to this document that have been posted as of 06/18/2010 . If updates have been made to the opportunity synopsis, update information is provided below the synopsis."

7. GOLD NANOROD DELIVERY OF AN SSRNA IMMUNE ACTIVATOR INHIBITS PANDEMIC H1N1 INFLUENZA VIRAL REPLICATION: *"These findings suggest that further evaluation of biocompatible nanoplexes as unique antivirals for treatment of seasonal and pandemic influenza viruses is warranted."*

CB Daily Report

Chem-Bio News

TAMIFLU AND RELENZA EMERGENCY USE AUTHORIZATION DISPOSITION LETTERS AND QUESTION AND ANSWER ATTACHMENTS

US Food and Drug Administration

June 22, 2010

"During the 2009 H1N1 influenza public health emergency, FDA issued Emergency Use Authorizations (EUAs) that authorized certain unapproved uses of Tamiflu and Relenza.

On June 21, 2010, the U.S. Food and Drug Administration (FDA) notified the Centers for Disease Control and Prevention (CDC) that these EUAs will terminate when the Public Health Emergency determination for 2009 H1N1 Influenza expires on June 23, 2010. Therefore, after June 23, 2010, the EUAs authorizing the unapproved uses of Tamiflu and Relenza will no longer be in effect."

.....

"ATTACHMENT 2

Update Regarding Stockpiled Antivirals at or Nearing Expiration

During the 2009 H1N1 influenza public health emergency, the FDA issued Emergency Use Authorizations (EUAs) authorizing the emergency use of certain expired lots of Tamiflu (oseltamivir phosphate) and Relenza (zanamivir) based on scientific review and analysis that found the drugs could be used beyond their labeled expiration dates.

On June 21, 2010, the U.S. Food and Drug Administration (FDA) notified the Centers for Disease Control and Prevention (CDC) that these EUAs for Tamiflu and Relenza will terminate when the Public Health Emergency determination for 2009 H1N1 Influenza expires on June 23, 2010. Therefore, after June 23, 2010, the emergency use of certain expired lots of Tamiflu and Relenza will no longer be authorized under the EUAs.

This statement provides CDC updated information regarding these identified lots for purposes of informing public health authorities. This statement is not directed to individual patients who already have Tamiflu and/or Relenza in their homes. If they have Tamiflu or

Relenza in their homes with expired date, they should discard the product.

For additional information, contact FDA's Division of Drug Information at 1-888-463-6332."

The full article can be found at: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm216249.htm>

[Return to Top](#)

WHO SEES POCKETS OF PANDEMIC FLU AND MORE H3N2

By Lisa Schnirring

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)

June 25, 2010

"Pandemic flu activity remained low in most parts of the world, though some areas such as Caribbean countries continued to see active transmission, with increased activity reported in a few areas, including Colombia and parts of India, the World Health Organization (WHO) said today.

After rising throughout winter and spring, levels of influenza B transmission throughout the world are decreasing, while influenza A (H3N2) viruses are increasing in some areas such as East Africa and South America, according to the WHO.

In a virological update that accompanied its weekly influenza report today, the WHO said overall, in the Northern Hemisphere, influenza B detections exceed that of influenza A. In the Southern Hemisphere, the proportion of influenza A (H3N2) is increasing, even exceeding that of pandemic H1N1."

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/jun2510global.html>

[Return to Top](#)

A NOVEL ANTI-INFLUENZA COPPER OXIDE CONTAINING RESPIRATORY FACE MASK

By Gadi Borkow, Steve S. Zhou, Tom Page, Jeffrey Gabbay

PLoS One

June 25, 2010

"Background

Protective respiratory face masks protect the nose and mouth of the wearer from vapor drops carrying viruses or other infectious pathogens. However, incorrect use and disposal may actually increase the risk of pathogen transmission, rather than reduce it, especially when masks are used by non-professionals such as the lay public. Copper oxide displays potent antiviral properties. A platform technology has been developed that permanently

introduces copper oxide into polymeric materials, conferring them with potent biocidal properties.

Methodology/Principal Findings

We demonstrate that impregnation of copper oxide into respiratory protective face masks endows them with potent biocidal properties in addition to their inherent filtration properties. Both control and copper oxide impregnated masks filtered above 99.85% of aerosolized viruses when challenged with 5.66 ± 0.51 and 6.17 ± 0.37 log₁₀TCID₅₀ of human influenza A virus (H1N1) and avian influenza virus (H9N2), respectively, under simulated breathing conditions (28.3 L/min). Importantly, no infectious human influenza A viral titers were recovered from the copper oxide containing masks within 30 minutes (≤ 0.88 log₁₀TCID₅₀), while 4.67 ± 1.35 log₁₀TCID₅₀ were recovered from the control masks. Similarly, the infectious avian influenza titers recovered from the copper oxide containing masks were $\leq 0.97 \pm 0.01$ log₁₀TCID₅₀ and from the control masks 5.03 ± 0.54 log₁₀TCID₅₀. The copper oxide containing masks successfully passed Bacterial Filtration Efficacy, Differential Pressure, Latex Particle Challenge, and Resistance to Penetration by Synthetic Blood tests designed to test the filtration properties of face masks in accordance with the European EN 14683:2005 and NIOSH N95 standards.

Conclusions/Significance

Impregnation of copper oxide into respiratory protective face masks endows them with potent anti-influenza biocidal properties without altering their physical barrier properties. The use of biocidal masks may significantly reduce the risk of hand or environmental contamination, and thereby subsequent infection, due to improper handling and disposal of the masks.”

.....

“Discussion

Based on a recently developed platform technology [24], [28], copper oxide particles were incorporated into 3 of 4 non-woven layers that comprise N-95 respiratory masks or Type IIR FFP1-level medical/patient respiratory masks. As demonstrated here in tests designed to simulate consumer use, the inclusion of the copper oxide particles in N-95 respiratory masks did not alter their physical filtration properties (Tables 1 and 3), but did endow them with the capacity to readily kill the virions that remain in the mask (Table 2). This is of major significance as the high viral titers that remain infectious in regular masks, as demonstrated in the control masks used in this study, can be a source of viral transmission both to the mask wearers and to others, as recently pointed out by the WHO [10].”

.....

“The mechanisms of virus kill are achieved via the interaction of copper ions with the virions that are entrapped in the mask or that come into contact with the surface of the copper oxide impregnated outer surfaces of the masks. The exact copper viral kill mechanisms need to be deciphered. The capacity of copper ions to render influenza virions, including H1N1 and H9N2 viruses, non-infective has already been demonstrated [26], [27], [30].”

Interestingly, it was found that the infectivity of H9N2 virus was reduced in a dose dependent manner at lower concentrations in which neither neuraminidase (NA) nor hemagglutination inhibition occurred [26]. Electron microscopic analysis revealed morphological abnormalities of the copper-treated H9N2 virus, but the exact kill mechanism was not elucidated [26].

Importantly, in addition to the antiviral properties of the copper oxide containing masks, the layers containing the copper oxide also have potent antimicrobial properties (data not shown), in accordance with the already reported broad-spectrum antimicrobial properties of fibers and fabrics containing copper oxide [24], [28], [29]. A lesser infectious bacterial load in an antimicrobial surgical respirator would at least reduce the risk of one potential source of nosocomial infections.

Could the addition of copper oxide into the masks result in an unsafe product for use? Several tests carried out in independent laboratories using good laboratory practices, which are not detailed in this report, have clearly shown that such is not the case.....”

The full article can be found at: <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0011295>

[Return to Top](#)

SIMULTANEOUS TYPING AND HA/NA SUBTYPING OF INFLUENZA A AND B VIRUSES INCLUDING THE PANDEMIC INFLUENZA A/H1N1 2009 BY MULTIPLEX REAL-TIME RT-PCR

Medical Letter on the CDC & FDA

June 20, 2010

“Here, such a multiplex real-time RT-PCR (rRT-PCR) assay for typing influenza A and B viruses and the pandemic influenza A/H1N1 2009 is developed. This assay can also subtype seasonal influenza A viruses simultaneously. The analytical sensitivity is 10-10(4) copies/reaction. The coefficients of variation of inter-assay and intra-assay are 0.04-0.45% and 0.08-0.97%, respectively. The new multiplex rRT-PCR assay is more sensitive in subtyping seasonal influenza viruses than the conventional PCR techniques. Results obtained with this assay for the detection of pandemic influenza A/H1N1 2009 are highly consistent (96.88%) with those achieved using the US CDC's rRT-PCR protocol. A sample identified as 'pandemic influenza A/H1N1 2009 positive' by the US CDC's rRT-PCR was reclassified correctly as subtype H3N2 using this assay.”

The full article can be found at: (Y. Yang, et. al., “Simultaneous typing and HA/NA subtyping of influenza A and B viruses including the pandemic influenza A/H1N1 2009 by multiplex real-time RT-PCR”. *Journal of Virological Methods*, 2010; 167(1): 37-44). Link not available.

[Return to Top](#)

EVALUATION OF QUICKVUE INFLUENZA A PLUS B RAPID TEST FOR DETECTION OF PANDEMIC INFLUENZA A/H1N1 2009

Life Science Weekly

June 22, 2010

"In the Philippines, pandemic influenza A/H1N1 2009 was first detected in May 2009 and by July 2009, 3207 cases and 6 deaths were reported. Using RT-PCR as the gold standard, clinical sensitivity/specificity of Quidel QuickVue (QV) influenza A+B was estimated across all age groups for pandemic influenza A/H1N1 using nasal swabs in a hospital setting. Effect of age, viral titers (Ct values), and timing of collection on QV sensitivity to detect pandemic influenza A/H1N1 2009 was also determined. Febrile patients with influenza-like illness (n=360) at the V. Luna General Hospital, Manila from 1 June to 31 August 2009 were included. Nasal swabs were tested using QV and RT-PCR. Of 360 nasal specimens 226 (63%) were positive for pandemic influenza A/H1N1. QV sensitivity was 63% (95% confidence interval (CI): 56-69%), specificity was 96% (95% CI: 91-99%), positive predictive value was 97% (CI: 93-99%), and negative predictive value was 57% (95% CI: 49-64%). Patient's age, fever severity, presenting symptoms or number of symptoms did not significantly affect QV sensitivity, however QV sensitivity was correlated with decreasing Ct values. QuickVue demonstrated moderate sensitivity for pandemic influenza A/H1N1 infection."

"There was a significant inverse association between Ct values and QV sensitivity for pandemic influenza A/H1N1."

The full article can be found at: (J.M.S. Velasco, et. al., "Evaluation of QuickVue influenza A plus B rapid test for detection of pandemic influenza A/H1N1 2009". Journal of Clinical Virology, 2010; 48(2): 120-122). Link not available.

[Return to Top](#)

DEVELOPMENT AND SUSTAINABLE MANUFACTURING OF ADJUVANTED PANDEMIC INFLUENZA VACCINES IN DEVELOPING COUNTRIES

BARDA, Assistant Secretary for Preparedness and Response, HHS

June 18, 2010

Document Type: Modification to Previous Grants Notice

Funding Opportunity Number: EP-IDS-10-003

Opportunity Category: Discretionary

Posted Date: Jun 18, 2010

Creation Date: Jun 18, 2010

Original Closing Date for Applications: Jul 23, 2010

Current Closing Date for Applications: Jul 23, 2010

Archive Date: Aug 22, 2010

Funding Instrument Type: Cooperative Agreement

Category of Funding Activity: Other (see text field entitled "Explanation of Other

Category of Funding Activity" for clarification)

Science and Technology and other Research and Development

Category Explanation: Development and Sustainable Manufacturing of Adjuvanted Pandemic Influenza Vaccines in Developing Countries

Expected Number of Awards:

Estimated Total Program Funding:

Award Ceiling: \$2,000,000

Award Floor: \$650,000

CFDA Number(s): 93.360 -- Biomedical Advanced Research and Development Authority (BARDA), Biodefense Medical Countermeasure Development

Cost Sharing or Matching Requirement: No"

.....

".....Strategies that can be implemented by influenza vaccine manufacturers in developing countries unencumbered by intellectual property restrictions and whose platform is not tied to a specific manufacturer or product would be highly advantageous in developing countries. For an antigen sparing strategy to contribute to global pandemic preparedness and response, that technology must be: 1) effective in decreasing the amount of vaccine antigen required to induce a protective immune response; 2) licensed and available at the time of the pandemic; and 3) feasible for implementing a mass vaccination program. Unfortunately, developing countries do not have access to appropriate adjuvant technology in their pandemic influenza development and manufacturing."

The full article can be found at: <http://www.grants.gov/search/search.do?mode=VIEW&oppld=55315>

[Return to Top](#)

GOLD NANOROD DELIVERY OF AN SSRNA IMMUNE ACTIVATOR INHIBITS PANDEMIC H1N1 INFLUENZA VIRAL REPLICATION

Biotech Week
June 30, 2010

"Here, we introduce a nanotechnology approach for the therapy of pan-demic and seasonal influenza virus infections. This approach uses gold nanorods (GNRs) to deliver an innate immune activator, producing a localized therapeutic response. We demonstrated the utility of a biocompatible gold nanorod, GNR-5'PPP-ssRNA nanoplex, as an antiviral strategy against type A influenza virus. In human respiratory bronchial epithelial cells, this nanoplex activated the retinoic acid-inducible gene I (RIG-I) pathogen recognition pathway, resulting in increased expression of IFN-beta and other IFN-stimulated genes (ISGs) (e.g., PKR, MDA5, IRF1, IRF7, and MX1). This increase in type I IFN and ISGs resulted in a decrease in the replication of H1N1 influenza viruses."

"These findings suggest that further evaluation of biocompatible nanoplexes as unique antivirals for treatment of seasonal and pandemic influenza viruses is warranted."

The full article can be found at: (K.V. Chakravarthy, et. al., "Gold nanorod delivery of an

ssRNA immune activator inhibits pandemic H1N1 influenza viral replication". Proceedings of the National Academy of Sciences of the United States of America, 2010; 107(22): 10172-7). Link not available.

[Return to Top](#)

END of CB Daily Report.

Send subscription requests, unsubscribing requests, questions and comments to:

Steve Tesko: Steve.Tesko@anser.org

Copyright 2008. *Analytic Services Inc.*

[Analytic Services Inc. DMCA Copyright Notice: http://www.homelandsecurity.org/bulletin/Draft_ANSER_DCMA_Copyright_Notice.htm](http://www.homelandsecurity.org/bulletin/Draft_ANSER_DCMA_Copyright_Notice.htm)

Use of these news articles does not reflect official endorsement.

In accordance with Title 17 (USC), Section 107, this material is distributed without profit or payment and is intended for nonprofit research and educational purposes only.

Reproduction for private use or gain is subject to original copyright restrictions.

PRIVACY POLICY

Content provided in the *CB Daily Report* does not reflect the viewpoint(s) of Analytic Services Inc. Analytic Services Inc. does not share, publish, or in any way redistribute subscriber email addresses or any other personal information.