出國報告（出國類別：其他會議）

赴葡萄牙阿爾布費拉參加第五屆流感疫苗國際會議「Influenza Vaccines for the World- IVW2015」

服務機關：行政院衛生福利部疾病管制署

姓名職稱：新興傳染病整備組 組長　楊靖慧

派赴國家：葡萄牙

出國期間：104 年 10 月 4 日至 10 月 11 日

報告日期：104 年 11 月 2 日

摘　　要

流感疫苗國際會議（Influenza vaccine for the world, IVW2015）每三年召開一次，此會議著眼於「流感疫苗相關議題 」，本次為第五屆會議，會議的專家委員會和學院成員包括了目前世界上流感疫苗領域第一線的專家。此次共計有 130 人，包括各國代表、學者專家(如公共衛生、醫療與獸醫相關等)與疫苗廠商代表等共襄盛舉。會議進行的模式是分成 11 個主題段落，內容以流感疫苗為主，從流感病毒的基礎研究、疫苗病毒株的製備、效力檢測、不同劑型的製造新技術以及提升產能等議題，尤其各個生技公司均將其研發的最新進度在會議中報告，讓與會者對流感疫苗的研發進展與最新研究均有完整的了解。本人代表疾病管制署參加本次會議，並發表一篇口頭報告(The experience of A/H5N1 vaccine immunization program in Taiwan and investigations on vaccine adverse events)及一篇海報論文(Evaluating the Stockpile and Usage Strategy of Vaccines and Antiviral Drugs during Seasonal and Pandemic Influenza.)。

目　　次

壹、背景說明與開會目的

2015 年流感疫苗國際會議（Influenza vaccine for the world, IVW2015）為此流感疫苗系列會議中的第五屆會議，每三年召開一次，此會議著眼於「流感疫苗相關議題 」，與另兩個主要的流感會議:歐洲學術工作小組流感研討會(European Scientific Working group on Influenza, ESWI)和流感防治年會（Options for the Control of Influenza）並列為流感相關的三大國際會議。

IVW 系列會議為國際論壇形式，讓世界著名的學者針對流感疫苗與相關議題（例如佐劑/遞送/接種策略等），報告其最新的研究結果，並且讓研究單位來報告最新的流感疫苗/技術相關的研發趨勢及目前的應用情形。此會議的專家委員會和學院成員包括了目前世界上流感疫苗領域第一線的專家與領袖。各國代表、學者專家(如公共衛生、醫療與獸醫相關等)與疫苗廠商代表等均共襄盛舉，一起來討論此重要議題。

為了解國際最新國際流感疫苗研究新進展，掌握流行趨勢及現況，增進專業職能，並且與各國代表交換流感防治相關經驗與策略，藉此檢視並修訂我國之流感防治相關政策，以期能應變瞬息萬變之流感疫情，由本人代表疾病管制署參加本次在葡萄牙阿爾布費拉市舉辦的第五屆流感疫苗國際會議，並代表疾病管制署新興傳染病整備組發表一篇口頭報告及一篇海報論文。

貳、行程表

日期	工作日誌	地　　點	行　程　內　容
104/10/04 104/10/05	啟程	台北→杜拜 杜拜→里斯本 里斯本→法魯機場 法魯機場→阿爾布費拉	路程（杜拜、里斯本轉機）； 抵達
104/10/06	報到	阿爾布費拉	赴大會報到
104/10/06 104/10/09	開會	阿爾布費拉	參加會議並發表論文
104/10/10 104/10/11	返程	阿爾布費拉→法魯機場 法魯機場→里斯本 里斯本→杜拜 杜拜→台北	路程（里斯本、杜拜轉機）
104/10/11	抵達	台北	抵達

參、會議過程介紹

此次共計有 130 人參加此為期 4 天的重要國際會議，會議的進行共分成 11 個主題段落，由與會學者專家進行口頭報告。於中間休息時間進行海報展示與討論。以下針對較重要的演講內容做介紹。

Session 1: Opening Plenary Session 1(10/6)

第一個講者是著名的病毒學家 John S. Oxford 教授，他介紹流感這 100 年來的歷史，從 1918 年的 Spanish influenza 到目前發展中的廣效型疫苗(universal influenza vaccine)。

第二位講者是美國威斯康辛州麥迪遜大學的 Yoshihiro Kawaoka 博士，他的研究主題是具有高產量能的流感疫苗病毒的發展。此研究的背景是因為在流感大流行時，需要快速且大量的製造流感疫苗，但是傳統的蛋胚培養技術不容易量產，目前最新的細胞培養技術可以使病毒抗原產量增加。若是能再利用新的技術使病毒在細胞培養時加速成長，則可以增加對於流感大流行時期大量疫苗需求的應變能力。Kawaoka 博士的團隊利用基因技術，發展出具有高產量能的流感疫苗病毒骨幹(high-yield influenza virus backbone)，其可以在細胞培養，甚至蛋胚培養時，增加 HA 抗原產量。此研究成果可以同時應用於流感大流行及季節流感疫苗的製作。

第三位講者是英國牛津大學的 Sarah Gilbert 教授介紹廣效型疫苗(universal influenza vaccine)的研發與進展。她指出目前季節流感疫苗的製造是從年初開始進行選株培養、六到七月進行效力檢測、八月進行充填包裝、九月運送至各國從十月開始施打，整個製作過程耗時頗長，然而這些保護抗體只能維持 3 到 6 個月。而這些傳統季節流感疫苗的效能只能算是普通，在 18 到 64 歲族群約為 59%，但在 65 歲以上族群僅達 35%。所以，近年來廣效型疫苗一直是最熱門的研究主題。何謂廣效型疫苗呢?可以是擴增宿主的免疫能力，例如對所有 A 型流感病毒皆有效，或是對特定 HA 抗原都有效(例如 H5 類 A 型流感病毒)，抑或是對於特定型別有效且能克服病毒變異(drift)的影響。此外，可以使抗體保護力的效期延長至 9 個月的疫苗，或是可以降低流感病人死亡率或病毒傳播能力的疫苗等，均是值得研發的方向。人體對抗流感病毒的武器，包括由 B 淋巴球產生針對流感病毒 HA 抗原部分的中和抗體，阻絕病毒表面 蛋白與宿主受器的結合，以阻止病毒

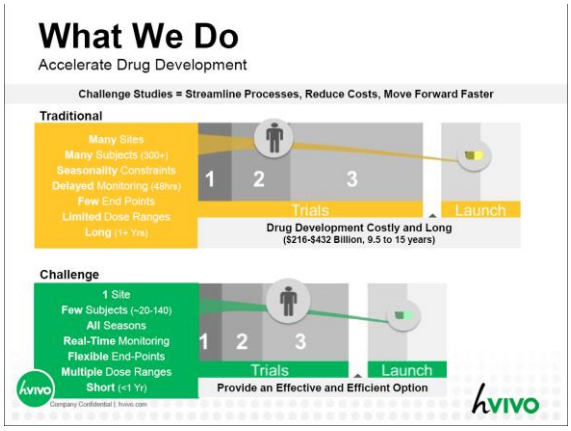
進入宿主細胞內；以及 T 細胞免疫，研究顯示人體 T 淋巴球能辨識流感病毒內部蛋白質的抗原部位，如核蛋白(nucleoprotein, NP)與基質蛋白(matrix protein, MP)，其產生的免疫反應可以降低或預防感染流感的症狀發生 (Natural T Cell-mediated Protection against Seasonal and Pandemic Influenza. Am J Respir Crit Care Med. 2015 Jun 15;191(12):1422-31)。而 NP 及 M2e 蛋白等為流感病毒內部較不易變異的結構部位，以此製造疫苗引發的 T 淋巴球免疫記憶具有交叉保護作用。利用改良的水痘病毒載體(Modified Vaccinia virus Ankara (MVA) vector)，附加上流感病毒的 NP 及 M1 蛋白抗原製成的的 MVA-NP+M1 疫苗已完成第一期與第二期臨床試驗，在健康成人與老年人均得到不錯的成效，是目前研發進度最快的廣效型疫苗之一(Berthoud et, al. Clinical Infectious Disease 2011)。除此之外，流感病毒 HA 抗原的軸柄部亦是比較穩定不易變異的構造，以此為基礎引發的中和抗體，可以對抗不同型別的流感病毒，目前亦有幾種疫苗研發進行中。

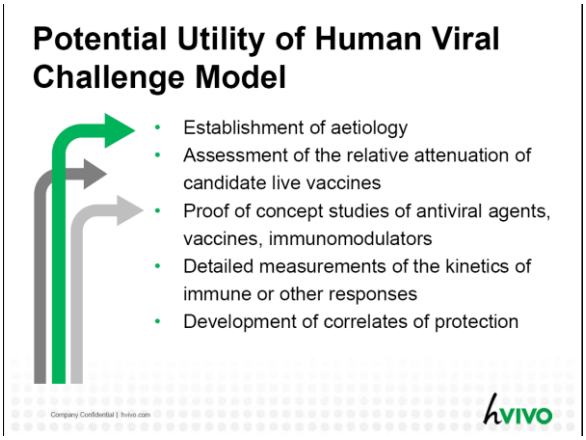
第四位講者是 David Fedson 教授，談的是除了流感疫苗外，可以增強宿主免疫力的一些藥物研究，例如 statin 此類降血脂藥物，研究顯示此類藥物可以重建內皮細胞的完整性(endothelial barrier intergrity)，進而降低流感病毒，甚至伊波拉病毒感染引起的敗血症，應該是一個可以值得繼續探討的方向。可惜大部分的科學家們對此議題沒有興趣，他呼籲科學家們應該保持開放的心胸來看待新的知識，才不會因為偏見而阻礙科技的進步。

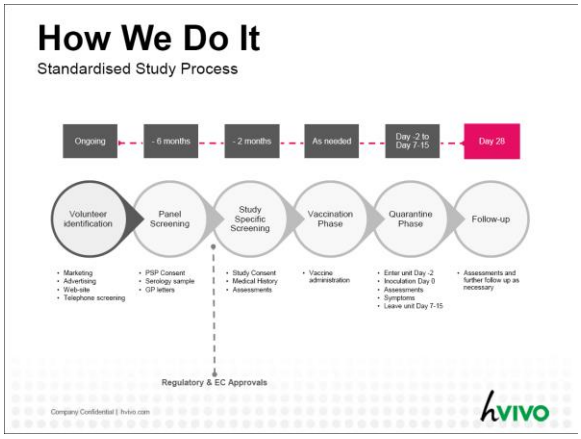
Session 2: Burden/Correlates of protection /Surveillance/ Potency (10/6)

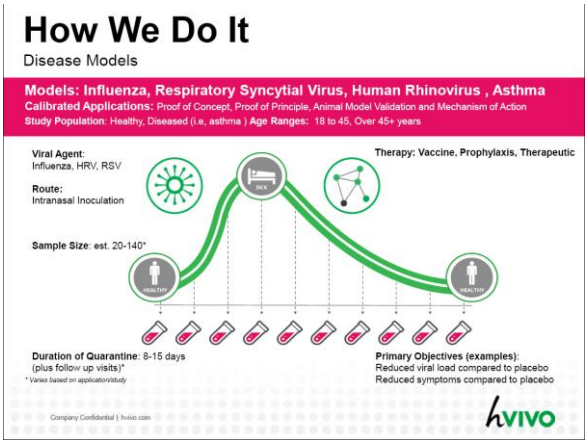
一共有六位講者，包括一些生技公司、研究團體，甚至是疫苗廠的研發部門來介紹新的研發成果，例如新型的疫苗效力測試(potency testing)，可以加速疫苗上市的速度，以便在流感大流行時盡快製造疫苗；利用分子生物技術來改變 H7N9 病毒的 Treg peptide，其可以增加引發抗體的能力等。其中比較有趣的是英國的 hVIVO 公司介紹其人體病毒挑戰實驗模式(Human virus challenge model，見下圖)，其設置了一個人體試驗中心，裡面設置 24 間負壓隔離病房並配置 24 小時輪值之醫療人員，整個試驗過程如下：招募受試者接臨床試驗，受試者需先進行健康檢查，再依研究設計進行特殊檢查或疫苗注射，之後入住病房隔離，於入住第二天進行病毒挑戰(即是利用病毒感染受試者)，受試者在試驗期間須隔離在病房裡 10-15 天，接受完整的生理監測與抽血檢驗(包含各種細胞激素、CD4 T 細

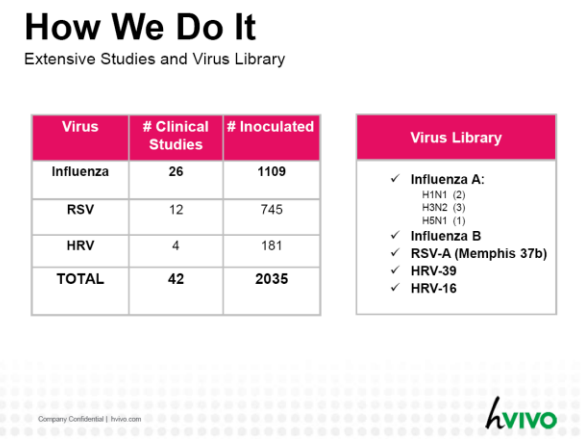
胞數目等)，機構內有嚴格的感染管制措施以避免交叉感染，出院後再繼續追蹤。此機構可以替藥物或疫苗研發單位進行病毒挑戰之人體試驗，跟傳統臨床試驗動輒 2000~4000 億美元的花費及 9.5-15 年的觀察時間相比，此模式可以有效率的快速進行測試，亦可以收集完整的檢體與資料，以供後續研究使用。該單位於第二天(10/7)的第四段落與第五段落時亦有相關的說明，其目前進行中的研究包含流感病毒、呼吸道融合病毒以及輪狀病毒等，迄今已進行超過 42 個臨床試驗，受試者達 200 人以上。不過此研究設備當然需要投資大量經費，並招募受試者等。











Session 3: Safety /Efficacy /Immunogenicity/ Potency (10/7))

第一部分是由蛋白質科學公司(Protein Sciences Corporation)的執行長 Manon M.J. Cox 博士介紹其最新的 Flublok 四價流感疫苗的研發成果。不同於當前的流感疫苗， Flublok 疫苗是利用基因工程製造出來的疫苗，將含有可以製造流感病毒 HA 抗原蛋白的昆蟲桿狀病毒(baculoviruses)植入裝載昆蟲細胞的反應器中，病毒會讓細胞群製造出所需要的 HA 抗原蛋白，進一步純化這些蛋白製成疫苗，其生產過程不會用到流感病毒或雞蛋。此新的製造技術允許在短時間內大量製造流感疫苗，傳統的蛋胚培養技術約需 6 個月才能製造出疫苗，而此技術僅需 1 個月，故在流感大流行時可以迅速應變。Flublok 三價流感疫苗在 2013 年 1 月獲得美國 FDA 核准上市，可以使用於 18 歲以上的成人。不過此疫苗的缺點是保存期限僅 6 個月，使用時須注意效期。Cox 博士在此次會議報告其四價流感疫苗的臨床試驗結果，受試者共計約 900 位 50 歲以上的成人，研究結果與傳統蛋胚培養製造的四價不活化流感病毒疫苗做比較，在保護力上顯示相當的效果，而副作用上則無差異。此四價疫苗預計在明年(2016)可以取得 FDA 核准上市。

另一位來自美國威斯康辛州大學的講者 Thomas C. Friedrich，利用全長基因定序的方法發現在雪貂傳播流感病毒試驗中，極少數含有變異位點的流感病毒仍具有傳染性，研究團隊並與一流感門診合作，納入 114 位流感病人做研究，發現有無接種疫苗對此變異性病毒的出現率並無相關，不過此變異病毒出現的機會並不高，因此其所扮演的角色與可能影響仍需進一研究。接著是 Sanofi Pasteur 公司來發表其肌肉注射型的不活化四價流感疫苗在 3 到 8 歲兒童的第三期臨床試驗結果，此臨床試驗地點有包含台灣。

Session 4: Influenza Vaccines/ Vaccination development I (10/7)

這部分是由一些生技公司來介紹一些新技術研發的流感疫苗，例如 Novavax 公司利用基因工程重組技術，針對病原體的關鍵性抗原製造出奈米粒子大小的類病毒蛋白(Virus-like protein, VLP)來製作疫苗，此種技術不只可以用在季節性流感疫苗，還可以用在新型流感病毒例如 H7N9 流感疫苗，甚至是伊波拉病毒疫苗。此外該公司亦利用自植物中提煉出的成分 Saponin，製成強效的疫苗佐劑 Matrix-M™，研究顯示其不僅可以增加抗體的產生，還可以引發 T 細胞的免疫反應，可以增加疫苗的效力。而 Eurocine Vaccines AB 公司則是致力於研發經鼻吸

入的不活化流感病毒疫苗。其研究背景是兒童使用注射型的不活化流感疫苗產生的免疫力比成人差一些，因為兒童多是未曾感染過，然而經鼻吸入的減毒活性流感疫苗在兒童的效果較佳，不過因為安全性考量，活性減毒疫苗無法使用於 2 歲以下的幼兒。該公司發展的經鼻吸入不活化流感病毒疫苗，已完成第一期與第二期臨床試驗，疫苗效力與安全性均得到不錯的結果，進一步的試驗要到 2016 年秋季才會完成。此外還有以利用基因重組技術去除 M2 蛋白基因的流感病毒製成的減毒活性疫苗(Flugen 公司)，在會議上報告動物試驗的成果良好，預計於 2016 年第一季進行第一期人體臨床試驗。INOVIO 公司研發的 DNA-based 流感疫苗，利用其研發的 SynCon® 質體來引發抗體產生與 T 細胞免疫，使疫苗的保護效果可以延長。此公司的研發項目除了季節及大流行流感疫苗外，還包括人體乳突狀病毒(HPV)、HIV、B 型肝炎病毒及伊波拉病毒等，目前亦準備開始進行第一期人體臨床試驗。最後是來自瑞典 Gothenburg 大學微生物免疫部門的 A. Omokanye 報告利用 Cholera toxin A1-subunit-ProteinA D-fragment fusion protein(CTA1-DD)作為輔助載體的流感疫苗在老鼠的實驗結果。

Session 5: Universal Influenza Vaccines (10/7)

一共有 5 位來自各國的專家發表其廣效型疫苗(universal influenza vaccine)的研發與進展，包括來自美國喬治亞大學的 Ted M. Ross 博士發表 COBRA(computationally optimized broadly reactive antigen) HA 疫苗等。內容較偏重技術面的介紹。

Session 6: Plenary Session II (10/7)

此場先由Bram Palache代表國際藥品制造商協會聯合會(International Federation of Pharmaceutical Manufacturers & Associations， IFPMA)來發表其自2008年起開始進行的全球流感疫苗劑量分佈的最新調查報告。雖然全球的流感疫苗總劑量數自2009年起逐年增加，但是歐洲地區與東地中海地區卻是呈現下降趨勢。疫苗劑量的分布可以視為是疫苗使用率的概估，由目前的劑量分佈報告顯示許多國家的季節性流感疫苗接種率(VCR)仍遠低於WHO設定的目標，也低於歐盟的建議目標。講者還特別提到去年印度在2014-2015流感季發生了H1N1大流行，造成近32,000人感染以及近2,000人死亡，對於一個人口數超過12億的國家，其流

感疫苗劑量分布低到令人無法置信。國際間與地區間的流感疫苗劑量分布差異顯示只靠WHO的呼籲與建議並無法達到目標，所以講者呼籲各國政府應該再採行其他的政策措施，特別是那些可以影響民眾疫苗接種意願(例如保險給付)與醫療人員促進疫苗接種意願(如對流感疫苗的知識、態度、行為和溝通)等，以達到提升季節性流感疫苗接種，保護大眾健康的目標。

第二位講者是來自歐盟CDC的Mike Catchpole博士，其呼應第一位講者，提到低流感疫苗接種率的原因，並說明與接種意願相關的阻礙，而醫療人員的推薦仍是目前研究顯示提高疫苗接種率最有效的方法。

第三位講者為Emanuele Montomoli，其主題是流感疫苗取得藥證之免疫檢測方式前景。基於流感的大流行風險，流感疫苗的藥證核准流程必須掌握速度。依據歐洲藥品管理局(EMA)的指引，傳統的檢測方式包括單相酶擴散法(single radial haemolysis，SRH)與血球凝集抑制抗體效價檢測(haemagglutination inhibition，HI)，此二方法在不同實驗室間會有相當的差異，需要再進行額外的條件來校正。因此EMA未來將引進新的方法，例如中和試驗(Micro Neutralization，MN test）和細胞免疫反應分析(cell- mediated immunity，CMI)，並標準化此二者與傳統檢驗結果的可比性，以便使目前的檢測評比量化。不過MN試驗的困難是若用於H5、H7等高風險禽流感病毒時，必須在生物等級第三級實驗室才能操作，若能使用influenza pseudotype HA作為抗原，則可以克服此缺點。

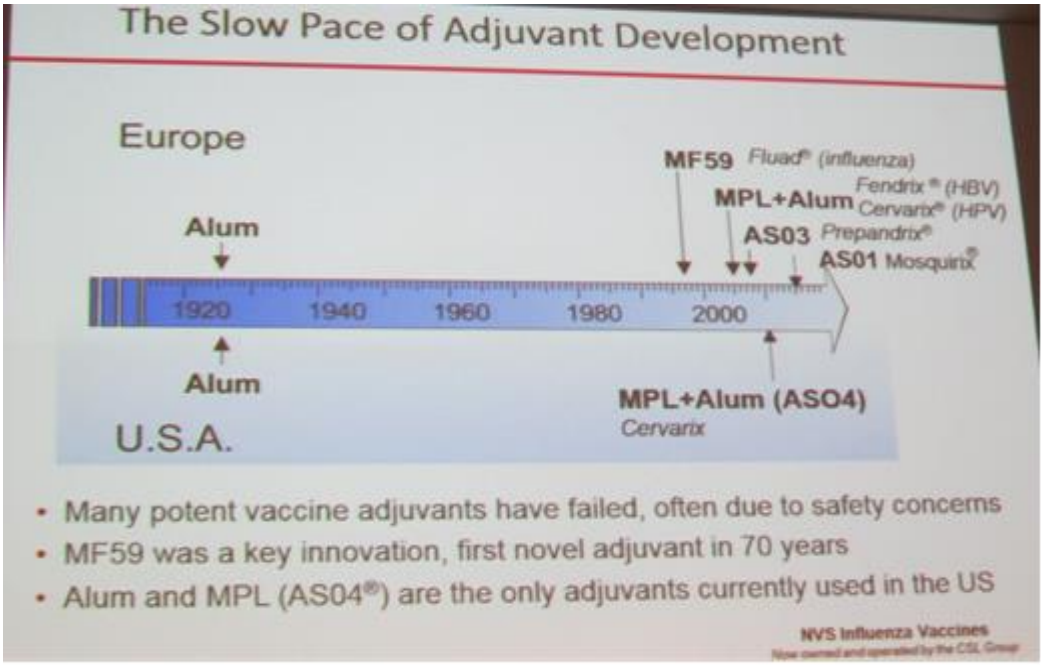
第四位講者是介紹EDUFLUVAC project，此研究是從各流感病毒株中選擇可能的HA與NA抗原，選定可以克服病毒變異(drift)的基因片段，將其植入桿狀病毒載體(baculovirus vectors)製成病毒蛋白疫苗，以便引發更多的抗體，講者主要是說明此類疫苗的研發與進展。

Session 7: Adjuvants, Formulation & Delivery (10/8)

第一位講者是來自芬蘭 Tampere 大學的 Timo Vesikari 教授，他主要是介紹佐劑在季節性與大流行流感疫苗的應用。有研究顯示兒童因為之前未得過流感，需要有較高的流感抗體，才能得到有效的保護力，而含有 MF59 佐劑的流感疫苗，比起無佐劑者可以在兒童產生較高的保護抗體。但是因為歐洲多個國家發生接種 Pandermix (其為因應 2009 年 H1N1 流感大流行生產的 H1N1 單價疫苗)引起猝睡症(narcolepsy)風險增加的事件，而此疫苗含有 ASO3 佐劑，因此所有含有佐劑的

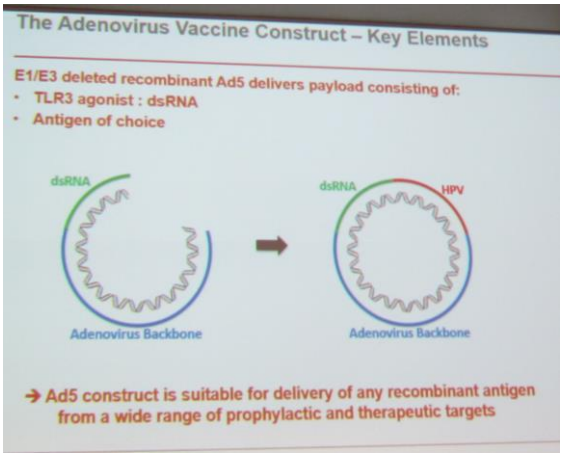
季節流感疫苗均未能取得歐盟核准給兒童使用，不過在美國與我國亦未核准含有佐劑的季節流感疫苗。但是講者認為 MF59 與 ASO3 構造不同，而且猝睡症只發生於 Pandermix 疫苗，該疫苗為裂解病毒製成，含有 NP，與一般季節流感疫苗不同。此外，中國亦曾報告接受不含佐劑的 H1N1 疫苗的猝睡症報告案例，表示 H1N1 流感病毒本身疫可能是原因。因此猝睡症可能是多種因素造成，其確切成因仍有待釐清。講者強調含有 MF59 佐劑的季節流感疫苗可以在年幼及年長這些流感高危險族群產生較高的保護力，目前因為媒體的大肆報導猝睡症相關新聞，使得施打率發生影響，更使得一些疫苗無法取得核准上市，這種現象是不好的，應該讓科學證據來說明，以免因噎廢食。不過講者亦提到含有佐劑的季節流感疫苗另一個需要注意的重點是佐劑每年施打是否會產生其他副作用，在小型的研究中只發現局部與全身性反應會略為加劇，缺乏長期且較大型的追蹤研究。

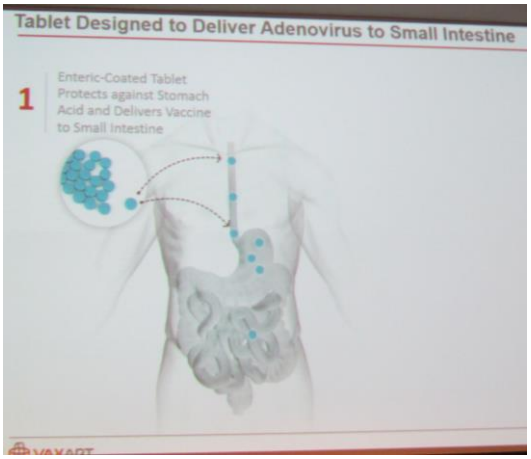
第二位講者是 CSL 疫苗廠(前諾華公司)的研發部門執行長 Manmohan Singh 介紹乳狀佐劑(emulsion based adjuvants)的歷史及其使用於流感疫苗的經驗(見下圖)。研究發現某些油脂(如礦物油)可以促進免疫反應，在抗原外圍包裹一層與水不互溶的油狀或乳狀物 (水包油形式)，可以使抗原緩慢釋放，增加抗體的產生。一般用在人體的疫苗佐劑以乳狀物為主，包括諾華公司研發的 MF59 與葛蘭素史克藥廠的 AS03。作者主要是介紹 MF59 的成分及其臨床試驗的結果。

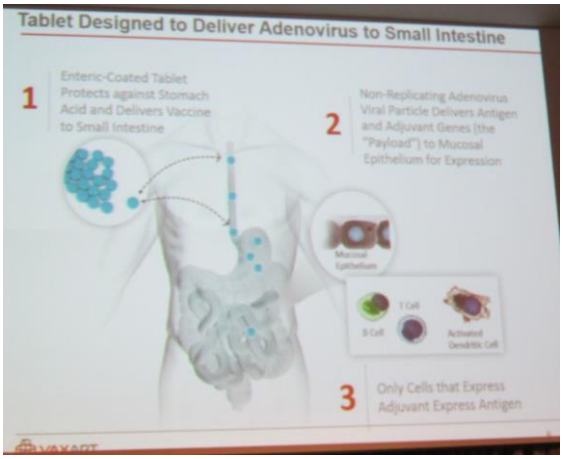


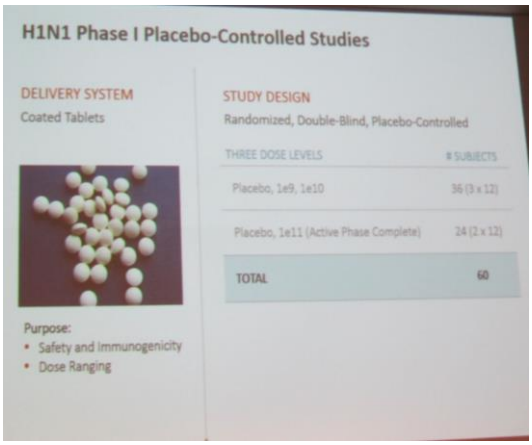
第三位講者是來自荷蘭的 Eva van Doorn 博士，介紹一個新的佐劑 ISA™51 之文獻分析。

第四位講者來自 VAXART 公司的 Sean Tucker，介紹一個非常有趣的口服錠劑型流感疫苗。該公司利用腺病毒作為載體，將病毒抗原附加在上面製成口服錠劑疫苗，錠劑進入腸胃道後可以在小腸刺激引發黏膜抗體產生，達到免疫效果(見下圖)。口服劑型的好處是保存方便，在常溫下可達一年，對於沒有疫苗冷藏設備(cold chain)的地區十分有利，且無注射處的局部反應。該公司之季節流感疫苗已進行第一期人體臨床試驗，一共有納入 79 位受試者，無特別不良反應。利用 MN 中合抗體試驗檢測，92%的受試者有 4 倍以上的抗體效價，目前試驗仍在繼續進行中。講完有專家提問其未來是否有打算將三種抗原一起放在同一錠劑上，不過講者回答是應該會分開，一種錠劑代表一種抗原，病人可以視需要選擇。

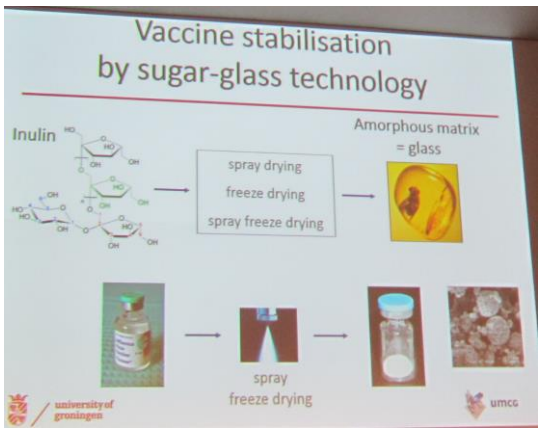


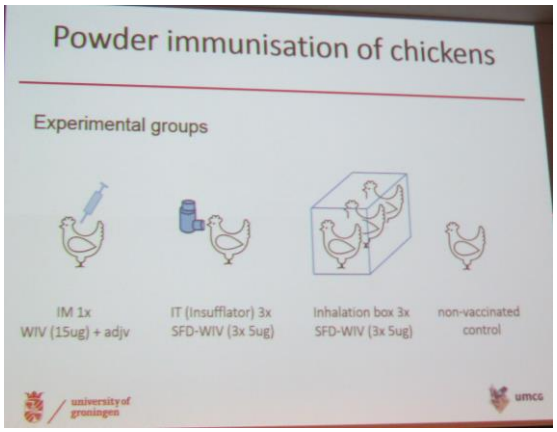






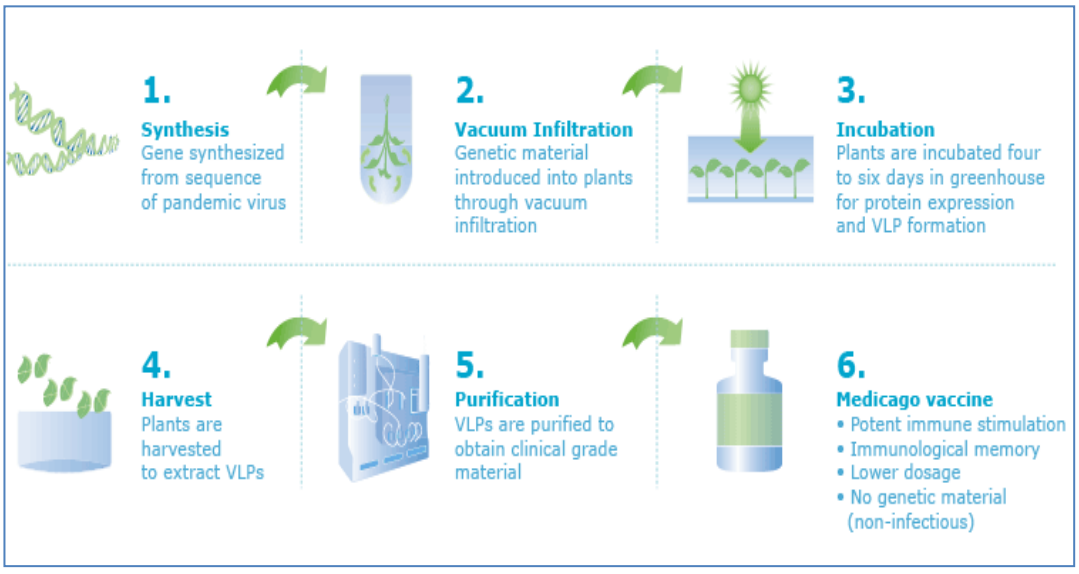
第五位講者 Anke Huckriede 博士介紹的是另一個有趣的疫苗型式--粉劑型式，利用 inulin 作為穩定劑，將目前非活化流感疫苗的凍晶改為可以在 30℃下儲存至少 3 個月的粉末，且維持其抗原性，粉末可以進一步製成舌下錠劑或吸入劑使用。其利用雞隻進行實驗，發現吸入型可以得到不錯效果，未來亦可以應用於家禽疫苗接種，不過其需要的濃度、時間與空間的條件仍待進一步的研究。





Session 8: Special Session (10/8)

這個段落是介紹 Medicago 公司，利用菸草葉製成的類流感病毒蛋白疫苗的研究成果。此技術之前曾運用於製造伊波拉病毒感染的抗體。利用植物製造流感疫苗的優點是菸草葉用以產生類病毒蛋白的技術已經發展多年，而菸草的大量繁殖與維持所需費用不高，而且整株植物均可以使用，產生的廢棄物料較少。目前該公司產品線中，大流行流感疫苗(H5 型別)的研發已完成第二期臨床試驗，而四價季節流感疫苗則剛完成第一期臨床試驗，結果均有不錯成效。



Session 9: Influenza Vaccines (10/8)

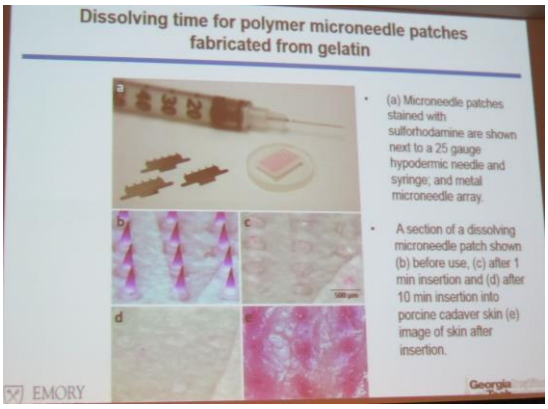
第一位講者的主題是減毒的大流行流感活病毒疫苗，減毒活疫苗的好處是所需的抗原量較低，而且對於輕微的病毒變異可能仍有保護效果，可惜講者因故未出席。另一個講者則是利用不同種類的猴子與猩猩來測試，發現 Cynomolgus macaque(食蟹猴)可以作為大流行 H1N1 流感病毒的動物實驗對象，因其在上呼吸道病毒增生的溫度與方式與人類較為相似。本人代表台灣疾病管制署在此段落報告我國 H5N1 疫苗接種計畫的執行情形以及相關的安全性結果，與會專家對於我國的研究成果十分有興趣，亦建議應該後續追蹤街中疫苗者的抗體變化。

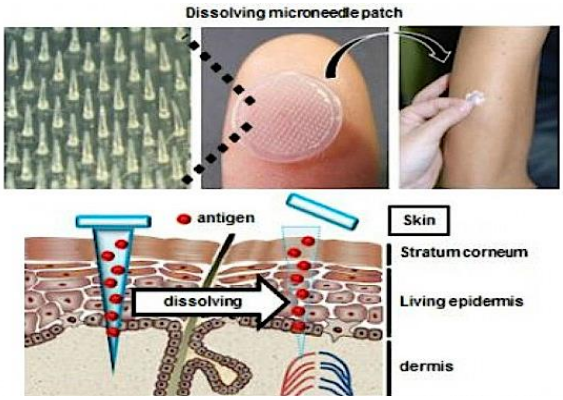
Session 10: Influenza Vaccines/Vaccination Development II (10/8)

第一位講者是 Medigen 公司的 Peter Pushko 博士介紹其基因重組之多亞型類病毒蛋白疫苗，其可以使宿主同時產生多種抗體以達到交叉保護的效果，此技術可用於流感大流行時快速製造疫苗。此次報告的是雪貂試驗的結果，顯示其產生的抗體可以同時對抗 H5N1、H7N2 與 H9N2 流感病毒的挑戰。另一位自日本的 Kuniaki Nerome 博士介紹其利用蠶蛹大量生產類流感病毒蛋白(VLP)的成果。

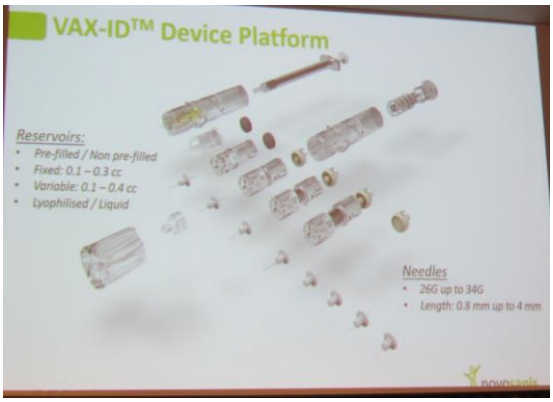
Session 11: Skin Vaccination (10/9)

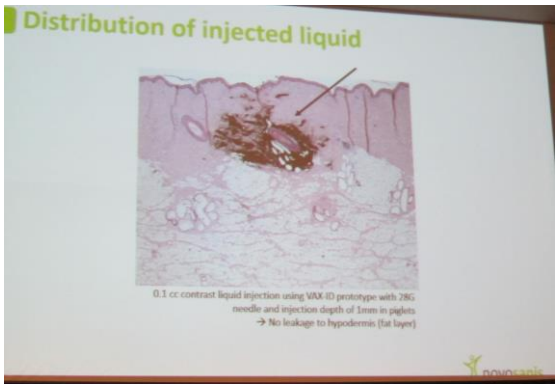
由來自美國 Emory 大學的 E. Stein Esser 博士介紹由其團隊發展出來的的細針皮膚貼片式(microneedle skin patch)流感疫苗的老鼠試驗結果。貼片疫苗上的細針不會帶來疼痛，傳遞藥物速率佳，且可自行使用，無須醫護人員協助；此外其所需的抗原量較少，可以在 25℃室溫儲存 80 天，上述均是其優於傳統肌肉注射型疫苗的特點。該團隊設計的細針是可溶解的，上面覆蓋流感病毒抗原，當貼片被敷在皮膚上時，微針就會刺穿皮膚的最表層，帶著疫苗一起溶解由表皮細胞吸收，達到產生抗體的效果。講者為了測試此疫苗在年幼及年長族群抗體產生的效果，設計了相對應的老鼠試驗。其選定 2 週大與 18 個月大的老鼠，比較貼片式與肌肉注射流感疫苗引發的抗體反應，結果二者沒有差異。此外講者又進行懷孕老鼠的試驗，結果亦是無差異，母鼠與生下來的幼鼠均可以產生抗體。該團隊之後準備進行人體試驗。





另一位講者是 Novosanis 公司的 Vanessa Vankerckhoven，介紹該公司生產的皮下注射型流感疫苗(VAX-ID™)。目前的進展是要測定不同部位的皮膚厚度，以取得最合適的針頭深度。





Session 12: Closing Session—Influenza Virus Strains (10/9)

此段落主要是介紹大流行 H1N1 流感病毒的一些基因分析。最後由 Ab Osterhaus 教授以禽流感病毒為總結，說明此人畜共通之傳染病的威脅仍持續中。

肆、心得與建議

本屆流感疫苗國際會議的內容相當的豐富，議程十分緊湊，每日從上午8時至下午19:30皆安排議程，一共包含11個段落，內容以流感疫苗為主，從流感病毒的基礎研究、疫苗病毒株的製備、效力檢測、不同劑型的製造新技術以及提升產能等議題，尤其各個生技公司均將其研發的最新進度在會議中報告，讓與會者對流感疫苗的研發進展與最新研究均有完整的了解，受益良多。

流感疫苗分為季節流感疫苗與大流行流感疫苗兩大類，兩者共通的困難是要在極短的時間內製造大量的疫苗，並且要能施注到廣大的族群中。前者要考慮的是目前的疫苗須每年施打，且在年幼與年長族群的保護效果略低，此外對於冷藏以及醫療設備不足的開發中國家，疫苗配送與接種計畫亦是重要議題。而後者則是需要快速製造出合格的疫苗，縮短審查與臨床試驗的時效性就相對十分重要。在此次研討會中，得知許多不同生技公司均投身於各種劑型及增加產量的流感疫苗研發，令人印象深刻。疫苗的研發需要投入大量的人力物力，但是其對人類的保護的效果遠大於其投資的金錢。台灣亦有先進的醫療技術與生物科技，可惜疫苗研發的產業相對發展較慢。此次會議，台灣僅有本人代表疾病管制署出席，沒有其他台灣代表參加，十分可惜，建議我國科技研發部門可以增派代表來出席此會議，以得到新知且激發新創意。

而此次研討會的另一個重點是在加速臨床試驗的時效性，有研究機構利用設置負壓病房、配置醫護人員並招募受試者入住隔離病房觀察等模式，加速臨床試驗的進行，但是當然需要投資大量經費。國內目前有多家醫學中心設置人體試驗中心，可以用來進行新藥的效果，不過缺乏此類呼吸道病毒挑戰人體模式，若國內能設置此研究中心，對我國的疫苗研發可以有很大的幫助，甚至可以拓展成為亞洲的試驗中心。

此次國際會議我國有一篇口頭報告與一篇海報論文的發表，增加我國在國際

間的能見度，但是因為只有一人與會，無法完整記錄與會過程。建議未來在經費許可下，可以增派人員參與此盛會，除了可以參觀其他國家的經驗外，也可進行國際衛生外交，拓展視野。

整體而言，由於我國自2005年起訂定「因應流感大流行整備計畫」，今年(2015年)為第二期計畫最後一年。此計畫有納入世界衛生組織規劃的相關的重點目標，依據此計畫，我國每年均投注大量人力物力進行整備，之間經過2009年H1N1流感大流行以及2013年中國H7N9流感疫情等事件，我國都能及時因應。不過在此二事件中亦發現我國對於流感疫苗研發與製造量能較為不足，相關的投資亦較為有限。目前國際間交通方便，人群往來活動頻繁，新興傳染病層出不窮，流感大流行的威脅更是一大隱憂。因此，我們除了必須持續監測國際疫情，隨時更新最新的疾病診斷技術外，更需掌握最新的疫苗研發知識，適時的引進新的疫苗，以期能保障台灣人民的健康與生命。

THE FIFTH INTERNATIONAL CONFERENCE & EXHIBITION ON:

INFLUENZA VACCINES FOR THE WORLD

6-9 October 2015, Sao Rafael Atlantic Hotel, Albufeira, Algarve, Portugal

FINAL ORAL PROGRAMME & POSTER PROGRAMME

IVW 2015

SCIENTIFIC ADVISORY PANEL

Othmar Engelhardt *(NIBSC/HPA, Potters Bar, UK)*
Eric Desauziers *(Sanofi-Pasteur, Lyon, France)*
John Oxford *(Queen Mary College London / hVIVO Ltd / Oxford Media & Medicine, London, UK)*
Albert Osterhaus *(University of Veterinary Medicine Hannover, Hannover, Germany)*
Ted Ross *(University of Georgia, Athens, Georgia, USA)*
Yoshihiro Kawaoka *(University of Wisconsin, Madison, Wisconsin, USA)*
Helen Bright *(MedImmune, Liverpool, UK)*
Jonathan Van Tam *(University of Nottingham, UK)*
Rob Lambkin-Williams *(hVIVO Ltd., London, UK)*
Dirk Poelaert *(GSK Vaccines, Wavre, Belgium)*
Ronald Kompier *(FluConsult, Noordwijk, The Netherlands)*
Keiji Fukuda *(WHO, Geneva, Switzerland)*
Manon Cox *(Protein Sciences Corporation, Meriden, Connecticut, USA)*
Emanuele Montomoli *(VisMederi Srl, Siena, Italy)*
Yotam Levin *(NanoPass Technologies Ltd, Rehovot, Israel)*
Manmohan Singh *(Novartis Influenza Vaccines, Holly Springs, North Carolina, USA)*
Anna-Karin Maltais *(Eurocine Vaccines AB, Solna, Sweden)*
Edward Remarque *(BPRC, Rijswijk, The Netherlands)*

10.30-12.30
Arrival, Registration, Poster & Exhibits Set-Up

12.30-13.30
Lunch, Posters & Exhibits

SESSION 1: OPENING PLENARY SESSION I

Moderator: Jonathan Van Tam *(University of Nottingham, Nottingham, UK)*

13.30-14.15
'From pneumococcus during the Spanish Influenza to EU universal influenza vaccines: A hundred years journey'
John S. Oxford
(Queen Mary College London / hVIVO Ltd / Oxford Media & Medicine, London, UK)

14.15-14.45
'Development of high-yield influenza vaccine viruses'
Yoshihiro Kawaoka *(University of Wisconsin, Madison, Wisconsin, USA)*

14.45-15.15
Keynote: 'Universal influenza vaccines: Designs and developments'
Sarah Gilbert *(University of Oxford, Oxford, UK)*

15.15-15.45
'Phenotypes, evolution and global public health: Treating the host response to pandemic influenza'
David Fedson *(Independent Consultant, Sergy Haut, France)*

15.45-16.00
Tea Break, Posters & Exhibits

SESSION 2: BURDEN/CORRELATES OF PROTECTION/SURVEILLANCE/POTENCY

Moderator: John S. Oxford
(Queen Mary College London / hVIVO Ltd / Oxford Media & Medicine, London, UK)

16.00-16.30
'Potency testing of inactivated influenza vaccines: An alternative potency assay using broadly reactive antibodies'
Chung Cheung and Othmar Engelhardt *(NIBSC, Potters Bar, UK)*

16.30-17.00
'Seasonal vaccination, burden of disease and the need for quadrivalent seasonal vaccines'
Dimitris Stefanidis *(GSK Vaccines R&D, Wavre, Belgium)*

17.00-17.30
'Correlates of protection to flu: What has the human viral challenge model revealed?'
Rob Lambkin-Williams *(hVIVO Ltd., London, UK)*

17.30-17.50
'H7N9 influenza T cell epitopes similar to human sequences are less immunogenic and may induce Treg-mediated tolerance: Implications for vaccine design'
Frances Terry and Annie De Groot
(EpiVax Inc./University of Rhode Island, Providence, Rhode Island, USA)

17.50-18.10
'Identification of the genetic signatures in the hemagglutinin (HA) protein that control the stability of live attenuated influenza vaccines'
Ruben Maeso, Alice Eaton, Zhongying Chen and Helen Bright
(MedImmune UK Ltd, Liverpool, United Kingdom)

18.10-18.30
'M2e-specific T Cell-engaging antibodies protect against Influenza A virus infection'
Kenny Roose[2,3], Jochen Pendzialek[1], Anouk Smet[2,3], Peter Kufer[1], Tobias Raum[1], Patrick A. Baeuerle[1], Markus Muenz[1], Xavier Saelens[2,3] and Walter Fiers[2,3] *(1 Amgen Research (Munich) GmbH, Munich, Germany; 2 VIB, Ghent, Belgium; 3 Ghent University, Ghent, Belgium)*

18.30-19.30
Posters Session & Exhibits

SESSION 3: SAFETY/EFFICACY/IMMUNOGENICITY/POTENCY

Moderator: Rob Lambkin-Williams *(hVIVO Ltd., London, UK)*

08.30-08.50

'Safety, efficacy, and immunogenicity of Flublok® in the prevention of season influenza in adults'

Manon M.J. Cox, Ruvim Izikson, Penny Post and Lisa Dunkle *(Protein Sciences Corporation, Meriden, Connecticut, USA)*

08.50-09.10

'Safety and immunogenicity of an intramuscular quadrivalent Influenza vaccine in children 3 to 8 years of age'

Stephanie Pepin [1], Henryk Szymanski [2], Ilya Angélica Rochín Kobashi [3], Sandra María Villagómez Martínez [4], José Francisco González Zamora [4], Jerzy Brzostek [5], Li-Min Huang [6], Cheng-Hsun Chiu [6], Po-Yen Chen [7], Anitta Ahonen [8], Aino Forstén [9], Edyta Miszczak-Kowalska [10], Ilkka Seppä [11], René Farfán Quiroz [12], Tiina Korhonen [13], Enrique Rivas [14], Celine Monfredo [1], Yanee Hutagalung [15] and Timo Vesikari [16] *(1 Sanofi Pasteur, Marcy l'Etoile, France; 2 St. Hedvig of Silesia Hospital, Poland; 3 Centro de Investigación Clínica del Pacífico, México; 4 Instituto Nacional de Pediatria, México; 5 Zespół Opieki Zdrowotnej, Poland; 6 National Taiwan University Hospital, Taiwan R.O.C.; 6 Chang Gung Children's Hospital, Taiwan R.O.C.; 7 Taichung Veterans General Hospital, Taiwan R.O.C.; 8 Helsinki South Vaccine Research Clinic, Finland; 9 Pori and Espoo Vaccine Research Clinics, Finland; 10 Independent Physician, Poland; 11 Turku Vaccine Research Clinic, Finland; 12 Hospital Infantil de Tlaxcala, México; 13 Tampere Vaccine Research Clinic, Finland; 14 Sanofi Pasteur, Mexico; 15 Sanofi Pasteur, Singapore; 16 University of Tampere Medical School, Finland)*

09.10-09.30

'Vaccine efficacy of Flublok® quadrivalent vs. IIV4 in Adults ≥50 years of age'

Manon M.J. Cox, Ruvim Izikson and Lisa M. Dunkle *(Protein Sciences Corporation, Meriden, Connecticut, USA)*

09.30-09.50

'Drugs influencing immune response and patient outcomes following influenza vaccination: A systematic review'

Subhadra Rajanaidu, Puja Myles and Jonathan Nguyen Van Tam *(University of Nottingham, Nottingham, UK)*

09.50-10.10

'Deep sequencing reveals potential antigenic drift variants at low frequency in influenza A-infected humans'

Thomas C. Friedrich, Nicholas W. Florek, Omolayo O. Fatola, Louise H. Moncla, James P. Mutschler, Jennifer K. Meece, Edward A. Belongia and Jorge M. Dinis *(University of Wisconsin-Madison, Wisconsin, USA)*

10.10-10.30

'VaxArray: A new analytical tool for influenza vaccine potency'

'Kathy L. Rowlen *(InDevR, Inc., Boulder, Colorado, USA)*

10.30-11.00

Coffee Break, Posters & Exhibits

SESSION 4: INFLUENZA VACCINES/VACCINATION DEVELOPMENT I

Moderator: Ted Ross *(University of Georgia, Athens, Georgia, USA)*

11.00-11.30

'Assessing the immunogenicity of influenza vaccines - both HA and NA are important'

Daryl Borley *(hVIVO Ltd, London, UK)*

11.30-11.50

'Vaccine platform in response to emerging infectious diseases: A/H7N9 flu and Ebola Zaire nanoparticles'

David Flyer and Gale Smith *(Novavax Inc., Gaithersburg, Maryland, USA)*

11.50-12.10

'Development of an inactivated nasal influenza vaccine'

'Anna-Karin Maltais *(Eurocine Vaccines AB, Solna, Sweden)*

12.10-12.30

'M2SR: A single replication next generation live influenza vaccine'

P. Bilsel, Y. Hatta, S. Sarawar, T.M. Ross, C. Crevar, A. Kelvin, D. Kelvin, D. Banner, S. Watanabe, G. Neumann and Y. Kawaoka *(Flugen Inc., Madison, Wisconsin, USA)*

12.30-12.50

'Broad cross-protective HAI responses induced by influenza consensus DNA vaccine'

Jian Yan, Matthew Morrow, Jaemi Chu, Janess Mendoza, Trina Racine, Amir S. Khan, Kate Broderick, Gary Kobinger, David B. Weiner and Niranjan Y. Sardesai *(INOVIO Inc., Plymouth Meeting, Pennsylvania, USA)*

12.50-13.10

'Development of a universal influenza vaccine based on the CTA1-DD adjuvant vector'

A. Omokanye [1], D. Grdic Eliasson [1], K. Schön [1], X. Saelens [2], W. Fiers [2] and N. Lycke [1] *(1 University of Gothenburg, Gothenburg, Sweden; 2 Ghent University, Ghent, Belgium)*

13.10-14.00

Lunch, Posters & Exhibits

SESSION 5: UNIVERSAL INFLUENZA VACCINES

Moderator: Manon Cox *(Protein Sciences Corporation, Meriden, Connecticut, USA)*

14.00-14.30

Keynote: 'Universal influenza vaccine challenges and hurdles'

Helen Bright *(AstraZeneca Biologics, Liverpool, UK)*

14.30-15.00

'Development of a universal influenza vaccine using the human viral challenge model'

Rob Lambkin-Williams *(hVIVO Ltd., London, UK)*

15.00-15.20

'Design and characterization of a universal H1N1 COBRA HA vaccine'

Ted M. Ross, Donald M. Carter, Christopher A. Darby, Bradford C. LeFoley, Cory J. Crevar, Timothy Alefantis, Stephen Anderson, Tod Strugnell, Guadalupe Cortes, Thorsten U. Vogel and Harold Kleanthous *(University of Georgia, Athens, Georgia, USA)*

15.20-15.40

'Infection-permissive immunity provided by NA- and universal M2e-based vaccines protects against influenza A virus challenge and allows the induction of heterosubtypic immunity during subsequent infections'

Michael Schotsaert, Tine Ysenbaert, Anouk Smet, Bert Schepens, Walter Fiers and Xavier Saelens *(Ghent University, Ghent, Belgium; Icahn School of Medicine at Mount Sinai, New York, USA)*

15.40-16.00

'The development of a universal live-attenuated H1N1 vaccine strain'

Ke Xu and Xianqiang Ping *(Institute Pasteur of Shanghai, Chinese Academy of Sciences, Shanghai, China)*

16.00-16.20

'Characterization of a stable trimeric influenza hemagglutinin stem as a broadly protective immunogen'

Harmjan Kuipers [1,5], Antonietta Impagliazzo [1,4], Fin Milder [1,5], Michelle Wagner [2,6], Xueyong Zhu [3], Ryan M.B. Hoffman [3], Ruud van Meersbergen [1,5], Jeroen Huizingh [1,5], Patrick Wanningen [1,5], Johan Verspuij [1,5], Martijn de Man [1,5], Zhaoqing Ding [2,6], Adrian Apetri [1,4], Basak Kükrer [1,4], Eveline Sneekes-Vriese [1], Danuta Tomkiewicz [1,4], Nick S. Laursen [3,7], Peter S. Lee [3], Anna Zakrzewska [1,5], Liesbeth Dekking [1,5], Jeroen Tolboom [1,5], Lisanne Tettero [1,5], Sander van Meerten [1,5], Wenli Yu [3], Wouter Koudstaal [1,4], Jaap Goudsmit [1,4], Andrew B. Ward [3], Wim Meijberg [1,5], Ian A. Wilson [3] and Katarina Radoševic [1,8]

(1 Crucell Vaccine Institute, Janssen Center of Excellence for Immunoprophylaxis, Archimedesweg 4-6, 2301 CA Leiden, The Netherlands; 2 Crucell Vaccine Institute, Janssen Center of Excellence for Immunoprophylaxis, 3210 Merryfield Row, San Diego, CA 92121, USA; 3 Dept. of Integrative Structural and Computational Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA; 4 Janssen Prevention Center, Janssen Pharmaceutical Companies of Johnson & Johnson, Archimedesweg 4-6, 2301 CA Leiden, the Netherlands; 5 Infectious Diseases and Vaccines Therapeutic Area, Janssen Research and Development, Janssen Pharmaceutical Companies of Johnson & Johnson, Archimedesweg 4-6, 2301 CA Leiden, The Netherlands; 6 Janssen Prevention Center, Janssen Pharmaceutical Companies of Johnson & Johnson, 3210 Merryfield Row, San Diego, CA 92121, USA; 7 Dept. of Molecular Biology and Genetics, Aarhus University, Gustav Wieds Vej 10C, Aarhus 8000, Denmark; 8 Global Biotherapeutics, Sanofi, 13 Quai Jules Guesde, 94400 Vitry-sur-Seine, France)

16.20-16.40

Tea Break, Posters & Exhibits

SESSION 6: PLENARY SESSION II

Moderator: John Oxford

(Queen Mary College London / hVIVO Ltd / Oxford Media & Medicine, London, UK)

16.40-17.10

'An IFPMA survey methodology to assess global influenza vaccine dose distribution: Latest data report'

Bram Palache *(IFPMA: International Federation of Pharmaceutical Manufacturers & Associations, Geneva, Switzerland)*

17.10-17.40

'Influenza vaccines: Where are we from a public health perspective?'

Mike Catchpole *(ECDC, Stockholm, Sweden)*

17.40-18.10

'Immunological analysis for influenza vaccines licensing, corresponding requirements from regulatory agencies and future perspectives'

Emanuele Montomoli and Simona Piccirella *(VisMederi srl, Siena, Italy)*

18.10-18.30

'EduFluVac project introduction and overview'

Edward Remarque *(BPRC, Rijswick, The Netherlands)*

18.30

Posters & Exhibits

FOR YOUR INFORMATION

Sixth ESWI Influenza Conference

10-13 September 2017, Riga, Latvia

More information will soon be available on www.eswiconference.org

SESSION 7: ADJUVANTS, FORMULATION & DELIVERY

Moderator: Ronald Kompier *(FluConsult, Noordwijk, The Netherlands)*

08.30-09.00
'Adjuvants in pandemic and seasonal influenza vaccines'
Timo Vesikari *(University of Tampere, Tampere, Finland)*

09.00-09.30
'History of emulsion based adjuvants and their use in influenza vaccination'
Manmohan Singh *(Novartis Influenza Vaccines, Holly Springs, North Carolina, USA)*

09.30-09.50
Safety and tolerability evaluation of the use of Montanide ISATM 51 as vaccine adjuvant: A systematic review'
Eva van Doorn, Heng Liu, Anke Huckriede and Eelko Hak
(University of Groningen, Groningen, The Netherlands)

09.50-10.10
'Oral tablet delivery induces systemic and mucosal antibody responses to influenza in humans'
Sean Tucker *(VAXART Inc., South San Francisco, California, USA)*

10.10-10.30
'Dry powder vaccines as a stable, effective and convenient alternative to parenteral influenza vaccines'
Anke Huckriede, Harshad P. Patil, Senthil Murugappan, Tjarko Meijerhof, Hendrik W. Frijlink and Wouter L.J. Hinrichs
(University of Groningen, Groningen, The Netherlands)

10.30-11.10
Coffee Break, Posters & Exhibits

SESSION 8: SPECIAL SESSION

'Advances in the clinical development of plant-made influenza VLP vaccines'
Moderator: Nathalie Charland
(Medicago Inc.,Sainte-Foy-Sillery-Cap-Rouge, Quebec, Canada)

11.10-11.40
'Plant-made VLP vaccines for influenza: The first 15 minutes'
Brian J. Ward *(McGill University, Montreal, Quebec, Canada)*

11.40-12.00
'Plant-made influenza VLP vaccines and the aging immune system'
Connie Michele Krawczyk *(McGill University, Montreal, Quebec, Canada)*

12.00-12.30
'Plant-made influenza VLP vaccines in the elderly: Clinical trial update'
Nathalie Landry *(Medicago Inc., Sainte-Foy-Sillery-Cap-Rouge, Quebec, Canada)*

12.30-13.30
Lunch Break, Posters & Exhibits

SESSION 9: INFLUENZA VACCINES

Moderator: Manmohan Singh
(Novartis Influenza Vaccines, Holly Springs, North Carolina, USA)

13.30-14.00
'The development of pandemic live attenuated influenza vaccines'
Helen Bright *(AstraZeneca Biologics, Liverpool, UK)*

14.00-14.30
'Efficacy and effectiveness of 2009 pandemic influenza A(H1N1)pdm09 vaccines: A systemic review and meta-analysis'
Louise E. Lansbury, Sherie Smith, Charles R. Beck and Jonathan S. Hguyen-Van-Tam *(University of Nottingham, Nottingham, UK)*

14.30-14.50
'Pandemic swine-origin H1N1 influenza virus replicates to higher levels and induces more fever and acute inflammatory cytokines in cynomolgus versus rhesus monkeys and can replicate in common marmosets'
Edmond J. Remarque, Petra Mooij, Gerrit Koopman, Daniella M. Mortier, Melanie van Heteren, Zahra Fagrouch, Rudy de Laat, Ivanela Kondova, Ernst J. Verschoor and Willy M.J.M. Bogers
(Biomedical Primate Research Centre, Rijswijk, The Netherlands)

14.50-15.10
'Characterization and development of replication competent DelNS1 live attenuated influenza vaccine for cross protection of heterosubtype influenza virus infection'
Honglin Chen, Min Zheng, Pui Wang, Wenjun Song, Siu-Ying Lau, Bobo Mok, Siwen Liu, Xiaofeng Huang and Kwok-Yung Yuen
(The University of Hong Kong, Hong Kong)

15.10-15.30
'The experience of A/H5N1 vaccine immunization program in Taiwan and an investigation on vaccine adverse events'
Chin-Hui Yang, Yun-Jui Shih, Li-Ching Hsu, Yi-Chien Chih and Shu-Mei Chou
(Center for Disease Control, Taipei, Taiwan, Republic of China)

15.30-16.00
Tea Break, Posters & Exhibits

SESSION 10: INFLUENZA VACCINES/VACCINATION DEVELOPMENT II

Moderator: Helen Bright *(AstraZeneca Biologics, Liverpool, UK)*

16.00-16.20
'Recombinant multi-subtype VLPs as broadly protective influenza vaccines'
Peter Pushko *(Medigen, Inc., Frederick, Maryland, USA)*

16.20-16.40
'The large-scale production of an artificial influenza virus-like particle vaccine in silkworm pupae'
Kuniaki Nerome [1], Shigeo Sugita [2], Kazumichi Kuroda [3], Sayaka Matsuda [1], Kei Majima [4], Kazunori Kawasaki [5] and Reiko Nerome [1] *(1 The Institute of Biological Resources, Nakayama, Nago, Okinawa 905-0004, Japan; 2 Equine Research Institute, Japan Racing Association, Tokami-cho, Utsunomiya, Tochigi 320-0856, Japan; 3 Division of Microbiology, Nihon University School of Medicine, Oyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan; 4 Baculotechnologies Co., Ltd., Hayashi-cho, Takamatsu, Kagawa 761-0301, Japan; 5 National Institute of Advanced Science and Technology (AIST), Midorigaoka, Ikeda, Osaka 563-8577 Japan)*

16.40-17.00
'Effects of egg-adaptation on receptor-binding and antigenic properties of influenza A (H3N2) vaccine viruses'
Lauren Parker, Stephen A. Wharton, Stephen R. Martin, Karen Cross, Yipu Lin, Yan Liu, Ten Feizi, Rodney S. Daniels and John W. McCauley
(The Francis Crick Institute, London, UK)

17.00-17.20
'Automated imaging and standardized interpretation of hemagglutination assays'
Kathy L. Rowlan *(InDevR, Inc.,Boulder, Colorado, USA)*

17.20
Posters & Exhibits

SESSION 11: SKIN VACCINATION

Moderator: To be confirmed

09.00-09.30

'Enhancing immune responses to influenza vaccines in high risk groups by skin vaccination'

E. Stein Esser [1], Dimitrios G. Koutsonanos [1,2], Sean R. McMaster [1], Priya Kalluri [3], Jeong-Woo Lee [3], Mark R. Prausnitz [3], Ioanna Skountzou [1,2], Timothy L. Denning [4], Jacob E. Kohlmeier [1,2] and Richard W. Compans [1,2] *(1 Department of Microbiology and Immunology and Emory Vaccine Center, Emory University School of Medicine, Atlanta, Georgia; 2 Emory-UGA Center of Excellence in Influenza Research and Surveillance, Emory University, School of Medicine, Atlanta, Georgia; 3 School of Chemical and Biomolecular Engineering, Georgia Institute of Technology, Atlanta, Georgia; 4 Institute of Biomedical Sciences, Center for Inflammation, Immunity and Infection, Georgia State University, Atlanta, Georgia)*

09.30-10.00

'VAX-ID™, platform of devices suited for accurate injection of small volumes in the dermis'

Vanessa Vankerckhoven *(Novosanis, Wijnegem, Belgium)*

10.00-10.20

'Assessing the economic and epidemiological impacts of a microneedle patch influenza vaccine'

Mercy Mvundura [2], Bruce Y. Lee [1], Sarah M. Bartsch [1], Courtney Jarrahian [2], Kristina M. Zapf [1], Kathleen Marinan [1], Angela R. Wateska [1], Bill Snyder [2], Savitha Swaminathan [2], Erica Jacoby [2], James J. Norman [3], Mark R. Prausnitz [3] and Darin Zehrung [2] *(1 Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; 2 PATH, Seattle, Washington, USA; 3 Georgia Institute of Technology, Atlanta, Georgia, USA)*

10.20-10.50

'Influenza microneedle vaccination platform enhances the protective immune responses against flu infection in pregnancy and increases longevity of passive immunity in offspring'

E. Stein Esser [1], Joanna A. Pulit-Penaloza [1], Haripriya Kaluri [2], Elena V. Vassilieva [1], Devin McAlister [2], Mark R. Prausnitz [2], Richard W. Compans [1] and Ioanna Skountzou [1] *(1 Emory University School of Medicine, Atlanta, Georgia, USA and 2 Georgia Institute of Technology, Atlanta, Georgia, USA)*

10.50-11.20

Coffee Break, Posters & Exhibits

SESSION 12: CLOSING SESSION – INFLUENZA VIRUS STRAINS

Moderator: Ab Osterhaus
(University of Veterinary Medicine Hannover, Hannover, Germany)

11.20-11.40

'Segment 2 from 2009pdm viruses confers temperature sensitivity on HA yield of candidate vaccine viruses in eggs'

S. Hussain [1], H.M. Wise [1], J.W McCauley [2], O. Engekhardt [3] and P. Digard [1] *(1 The Roslin Institute, University of Edinburgh, Edinburgh, UK; 2 The Francis Crick Institute, Mill Hill, London, UK; 3 National Institute for Biological Standards and Control, Potters Bar, UK)*

11.40-12.00

'Reverse genetic vaccine seeds for Influenza A(H1N1)pdm09: Source of PB1 as a determinant factor in virus growth and antigen yield'

Marta Gíria [1], Luís Santos [2], João Louro [2], Vanessa Correia [2] and Helena Rebelo de Andrade [1,2] *(1 Faculdade de Farmácia da Universidade de Lisboa, Lisboa, Portugal; 2 Instituto Nacional de Saúde Dr Ricardo Jorge IP, Lisboa, Portugal)*

12.00-12.40

'Avian influenza viruses: The Continued Threat'

Ab Osterhaus *(University of Veterinary Medicine Hannover, Hannover, Germany)*

12.40

Closing Remarks, Lunch & Departure

Poster 101
'Polyvalent influenza: A DNA vaccine for pigs using needle-free intradermal delivery'
Marie Borggren *et al.*
(Statens Serum Institut, Copenhagen, Denmark)

Poster 102
'Evaluating the stockpile and usage strategy of vaccines and antiviral drugs during seasonal and pandemic influenza'
Chia-Kun *et al.*
(Centers for Disease Control, Taipei, Taiwan, Republic of China)

Poster 103
'Design of randomized, double-blind, controlled, multi-center phase IIb trials as part of the EU-funded UNISEC project to assess the safety and immunogenicity of cross-seasonal universal influenza vaccines with or without pandemic influenza vaccine in healthy adults'
H. Liu *et al.*
(University of Groningen, Groningen, The Netherlands)

Poster 104
'Influenza NP-incorporating virosomes adjuvanted with MPLA as a new vaccine to induce cross-protective immunity to influenza virus'
Wei Dong *et al.*
(University Medical Center Groningen, University of Groningen, Groningen, The Netherlands)

Poster 105
'A human DC-based system to evaluate responses towards vaccines'
Gabriela Tapia *et al. (University Medical Center Groningen, University of Groningen, Groningen, The Netherlands)*

Poster 106
'Head-to-head comparison of liposome and protein based adjuvants combined with whole inactivated virus influenza vaccine (WIV) for induction of cross-reactive immunity in mice'
Yoshita Bhide *et al. (University Medical Center Groningen, University of Groningen, Groningen, The Netherlands)*

Poster 107
'Immunogenicity and efficacy against serologically evidenced influenza infections of 2014-15 influenza vaccine in elderly people living in nursing homes'
Barbara Camilloni *et al.*
(University of Perugia, Perugia, Italy)

Poster 108
'The morbidity and vaccination status of influenza in Russian Federation'
N.I. Briko and T.S. Saltykova
(I.M. Sechenov First Moscow State Medical University, Moscow, Russia)

Poster 109
'Mono- and trivalent immunoadjuvant influenza vaccines immunogenicity and safety in pregnant women'
N.I. Briko *et al.*
(I.M. Sechenov First Moscow State Medical University, Moscow, Russia)

Poster 110
'Inactivated or damaged? Comparing the effect of inactivation methods on influenza virions to optimize vaccine production'
Aurora Signorazzi *et al.*
(University of Groningen, Groningen, The Netherlands)

Poster 111
'Self-adjuvanting influenza candidate vaccine carrying HA stalk domain and M1 epitopes on a proteinaceous multivalent nanoplatform'
Inga Szurgot *et al.*
(Polish Academy of Sciences, Warsaw, Poland)

Poster 112
'Exposition of influenza A antigens on the surface of recombinant *Bacillus subtilis* endospores'
Bogus Szewczyk *et al.*
(University of Gdansk and Medical University of Gdansk, Gdansk, Poland)

Poster 113
'Pulmonary deposition of influenza vaccine formulations'
Jasmine Tomar
(University of Groningen, Groningen, The Netherlands)

Poster 114
'A comparison of cost effectiveness of seasonal influenza vaccines in Spain'
Eckhardt Petri *et al.*
(Novartis Influenza Vaccines Marburg GmbH, Marburg, Germany)

Poster 115
'Pathological changes in mice infected with a novel highly pathogenic avian influenza A(H5N8) virus in South Korea'
Chi-Kyeong Kim *et al.*
(Centers for Disease Control and Prevention, Chungcheongbuk-do, Republic of Korea)

Poster 116
'Development of a stable and fixed nucleotide length poly I:C "uPIC" as an adjuvant for vaccines'
Tetsuo Nakano and Tomoumi Nagai
(Kyowa Hakko Bio Co., Ltd., Yamaguchi, Japan)

Poster 117
'Optimization of influenza A vaccine virus by reverse genetic using chimeric HA and NA genes with an extended PR8 backbone'
Houda Boukhebza *et al.*
(Sanofi Pasteur, Marcy L'Etoile, France)

Poster 118
'The interactions between an antigen and adjuvant in influenza vaccine formulations'
P.A. Born *et al.*
(University of Groningen, Groningen, The Netherlands)

Poster 119
'An assessment of potential public health and economic benefits of quadrivalent influenza vaccine in comparison to trivalent vaccine in Australia 2002-2012'
B. Macabeo *et al.*
(Sanofi Pasteur, Lyon, France)

Poster 120
'Bacterially produced hemagglutinin protein protects chickens against challenge with highly pathogenic H5N1 influenza viruses'
V. Saczynska *et al.*
(Institute of Biotechnology and Antibiotics, Warsaw, Poland)

Poster 121
'Highly immunogenic antigens produced in *Pichia pastoris* as candidates for influenza subunit vaccine'
Konrad Zdanowski *et al.*
(University of Natural Sciences & Humanities, Siedice, Poland)

Poster 122
'Highly pathogenic avian influenza virus infection is associated with the pathogenesis of entheropathy in mice'
Hyuk Chu *et al.*
(Korea National Institute of Health, Chungbuk, Republic of Korea)

Poster 123
'Booster effect against old H1N1 influenza strains after flu seasonal vaccination'
R. Ortiz de Lejarazu *et al.*
(University Clinic Hospital of Valladolid, Valladolid, Spain)

Poster 124
'Heterologous response against avian flu strains after vaccination with trivalent seasonal flu vaccine'
R. Ortiz de Lejarazu *et al.*
(University Clinic Hospital of Valladolid, Valladolid, Spain)

Poster 125
'QIV versus TIV: Evidence-based impact of lineage mismatch on influenza B vaccine efficacy. An umbrella meta-analysis of published literature'
Walter E.P. Beyer *et al.*
(Viroscience, Erasmus Medical Centre, Rotterdam, The Netherlands)

Poster 126
'A latex agglutination assay (LAA) to quantify the amount of HA protein in A/H5N1 and A/H1N1 influenza monovalent vaccines'
Sophie Buffin *et al.*
(Sanofi Pasteur, Marcy L'Etoile, France)

Poster 127
'Alternative method development for quantification of haemaglutinin in influenza vaccine: Method comparing and monitoring study'
Hyunkyung Kang *et al.*
(NIFDS, Chungcheongbuk-do, Korea)

Poster 128
'Combining stable insect cell lines with baculovirus-mediated expression for production of multi-HA influenza VLPs'
Antonio Roldao *et al.*
(Instituto de Biologia Experimental e Tecnologica, Oeiras, Portugal)

Poster 129
'Tackling bottlenecks in IC-BEVS: Enhancing enveloped viral particles production by targeted supplementation design'
Francisca Monteiro *et al.*
(Instituto de Biologia Experimental e Tecnologica, Oeiras, Portugal)

Poster 130
'A click chemistry approach to monitor and improve influenza VLPs downstream processing'
S.B. Carvalho *et al.*
(Instituto de Biologia Experimental e Tecnologica, Oeiras, Portugal)

Poster 131
'Stability improvements to subunit and live attenuated influenza vaccines'
Marcus Estrada
(PATH, Seattle, Washington, USA)

Poster 132
'Detection of neuraminidase-inhibiting antibodies in human serum to complement evaluation of antibody response to A(H1N1)pdm09 virus infection'
Catherine Thompson *et al.*
(Public Health England, Colindale, London, UK)

Poster 133
'High throughput use of the haemagglutination inhibition assay during phase 3 clinical trials using large virus panels'
Daryl Borley *et al.*
(hVivo Services Ltd., London, UK)

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The experience of A/H5N1 vaccine immunization program in Taiwan and an investigation on vaccine adverse events

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Objective

To prepare for the emerging avian influenza pandemic, Taiwan implemented A/H5N1 vaccine (pre-pandemic vaccine) immunization program since 2007 for targeted personnel based on the SAGE recommendation. This study is to assess vaccine safety.

Methods

The targeted group for A/H5N1 vaccine in Taiwan included laboratory workers involving H5N1 virus, health care workers, public health personnel, customs immigration quarantine security (CIQS) personnel, poultry workers, and travelers who may travel to H5N1 virus affected areas. Vaccine strains used in the immunization period were different between years, which included Vietnam (Baxter/ Novartis), Indonesia (Baxter), and Turkey (Novartis) strains. Individuals were required to take two doses to complete vaccination, with the second dose be given after an interval of at least 3 weeks after the first dose. We collected 2007-2008 and 2010-2014, total 7 years' vaccination data for analysis. To monitor adverse events of vaccine, vaccinee were asked to complete a questionnaire within 7 days after vaccination. The questionnaire was not available in 2011-2012 and was excluded for analysis.

Results

A total of 56,700 doses of vaccine were administered during the vaccination period in the study period, the two doses coverage rate was 74.2% (24,154/32,546). There were 31,041 health care workers and 11,977 poultry workers, 888 laboratory workers vaccinated, accounted for 77.4% of total vaccinee. The estimated coverage rate was 6.1% among health care workers, 13.9% among poultry workers and over 90% among H5N1 virus related laboratory workers. There were 16,274 questionnaire (response rate: 71.1%) enrolled for adverse events study. The common adverse events were local reactions such as redness, swelling, pain, or itch at the injection site, reported by 21.7% of vaccinee, and 92.9% were relieved within 3 days. As to other events, there were 5.1% of vaccinee reported to have myalgia and 5.0% had fatigue. Nevertheless, 90.1% of the above systemic reactions relieved within 3 days.

Conclusion

The target groups, H5N1 virus related laboratory workers, poultry workers and health care workers had high A/H5N1 vaccination coverage rate. Moreover, the analysis also demonstrated the safety of A/H5N1 vaccine which no severe adverse event was observed in our program.

Keywords: H5N1 vaccine, Vaccine safety, Adverse events, Taiwan

Evaluating the Stockpile and Usage Strategy of Vaccines and Antiviral Drugs during Seasonal and Pandemic Influenza

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Background

Antiviral drug (AVD) is an important weapon for flu pandemic and epidemic, though the high cost and expiration duration was a big burden for large-scale and long-term national AVD stockpile for government. The overall AVD stockpile in Taiwan is about 10% of total population. To evaluate what proportion of AVD stockpile is appropriate and efficacious during flu pandemic, we conducted this study to estimate the cost-benefit and the effectiveness of the preparedness strategy.

Materials and Methods

This study use an individual-based stochastic disease simulation system to produce different levels of epidemic that similar to the country, the system was established by Taiwan Centers for Disease Control (CDC) and Institute of Information Science, Academia Sinica. In addition, we use Pharmaceutical Intervention (PI) real data including flu vaccine and AVD usage, and compare to other research references to set-up multi-strategy combinations used in the simulation. We estimate the cost-effectiveness of AVD stockpile and vaccination usage strategies within seasonal and pandemic influenza simulation. Each epidemic simulation was seeded by infecting 20 randomly individuals and the epidemic lasted for 270 days.

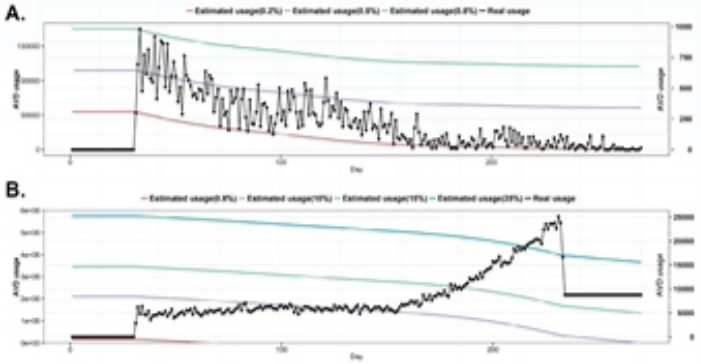

Figure 2. Simulation of different AVD stockpile value in Seasonal(A) & Pandemic(B). Y-axis: Estimated AVD usage (left), Real AVD usage (right)

Results

From the results, we found PI strategy combined Target Vaccination (TV) plus Targeted Prophylaxis (TAP) with stockpiled AVD (0.8% of total population) is the most cost-effective strategy to reduce the epidemic of seasonal influenza (R_0=1.27), the lowest stockpile threshold is 0.2% of population. For Pandemic influenza (R_0=1.60), Target vaccination (TV) plus Targeted Prophylaxis (TAP) with stockpile d AVD (10% of total population) is the most cost-effective strategy, the lowest stockpile threshold is 10% of total population.

Figure 1. Research structure

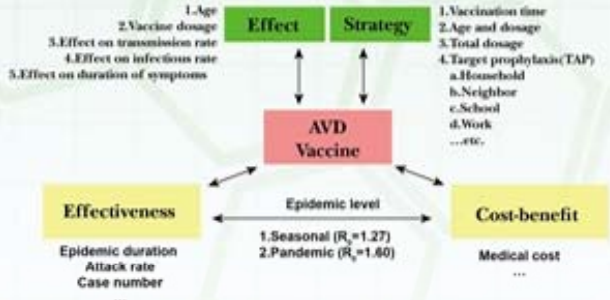

Table 1. Comparison of TV + TAP (0.8%) with Non in seasonal epidemic; TV + TAV (25%) with TV + TAP (10%) in pandemic.

	Seasonal		Pandemic	
	Non	TV + TAP (0.8%)	TV +TAV (25%)	TV +TAP (10%)
Sym.	5,702,239	524,810	-	-1,986,145
Hos.	50,377	5,081	-	-16,816
Death	10,530	546	-	-3,384
VC cost	0	314,916,580	298,500,000	298,500,000
AVD cost	0	114,065,000	3,747,850,000	1,368,780,000
DC cost	9,600,597,172	869,243,153	4,151,487,739	959,521,900
Total cost	9,600,597,172	1,298,224,733	8,197,837,739	2,626,801,900
Diff (Cost)	-	-8,302,372,439	-	-5,571,035,839
Benefit	0	178,012.12	-	63,059.51
ICER	-	Dominant	-	Dominant

Sym.:Symptomatic case
Hos.:Hospitalization
VC cost: Vaccine cost
DC cost: Direct cost

Conclusions

1.Seasonal: 1% of total population AVD usage + TV + TAP is the most cost-benefit strategy.
2.Pandemic: 10% of total population AVD stockpile + TV + TAP is the most cost-benefit strategy.
3.In fact, AVD has 7 year expiration duration and annual routine stockpile in Taiwan, while we release 1% AVD annually, we think it would cost lesser when Pandemic occurred.
4.Precision of simulation needed improve and could consider require multi-model estimating cost-benefit, thus cross-validation could make the results more reliable.