RESULT SUMMARY

Observational Influenza Vaccine Active Surveillance Study: A Phase IV Prospective Multi-Centre Cohort Study to Evaluate the Reactogenicity of bioCSL's Influenza Virus Vaccine (2015/2016 formulation)

Protocol No:	CSLCT-SAF-15-07
EU PAS/ENCePP register number	ENCEPP/SDPP/10613
Study Product:	2015/2016 Northern Hemisphere Formulation of Enzira (Split Virion, Inactivated Influenza Vaccine)
Sponsor:	bioCSL Pty Ltd.
Contact Details:	63 Poplar Road, Parkville VIC 3052 Australia Tel: +61 3 9389 2000
Indication Studied:	Prophylaxis of Influenza
Development Phase:	Phase IV
Study Initiation Date:	15 September 2015 (first participant enrolled)
Study Completion Date:	19 November 2015 (last participant completed)
Report Type:	Result Summary (based on CSR Final Version 1.0, dated 03 February 2016)
Author	Dr. Daphne Sawlwin Global Clinical Safety and Pharmacovigilance bioCSL PTY LTD / CSL LTD
Report Summary Date:	18 February 2016

Title	Observational Influenza Vaccine Active Surveillance Study: A Phase IV Prospective Multi-Centre Cohort Study to Evaluate the Reactogenicity of bioCSL's Influenza Virus Vaccine (2015/2016 formulation)
Keywords	Observational, active surveillance, influenza vaccine, multi-centre, cohort study
Rationale and background	The European Medicines Agency (EMA) has provided new interim guidance on enhanced safety surveillance for seasonal influenza vaccines focusing on signal detection for influenza virus vaccines licensed in Europe (EMA/PRAC/222346/2014). This interim guidance focuses on requirements and principles for annual enhanced safety surveillance, to rapidly detect any increased local and systemic reactogenicity that may arise during the influenza vaccine product life-cycle, such as may occur due to significant changes in the manufacturing process or that may potentially arise with updated influenza virus vaccine strains. This Post-Authorisation Safety Study (PASS) has specifically been conducted to meet the objectives of the interim guidance for the current European Union (EU)-licensed bioCSL Influenza Virus Vaccine (IVV) in the EU, for the influenza season 2015/2016.
Research question and objectives	This study describes an enhanced active surveillance system that collected participant self-reported reactogenicity data, which was supplemented by primary care or other health provider data on the details of vaccination, and any medically attended adverse events (MAEs) in the seven-day period after each bioCSL influenza vaccination. Descriptive summaries of the reactogenicity and other safety data allowed indirect comparison of data from the study with previous safety data and data arising from the enhanced safety surveillance system over time, to facilitate safety signal detection for bioCSL's IVV. *Primary objective* To characterise the reactogenicity (local, systemic and allergic reactions) occurring within seven days after each influenza vaccination with bioCSL's IVV in participants routinely indicated for influenza vaccination in specified age groups. *Secondary objective* To assess the frequency and severity of MAEs occurring within seven days after each influenza vaccination with bioCSL's IVV in participants routinely indicated for influenza vaccination in specified age groups.
Study design	People who had been, or were just about to be, routinely vaccinated with bioCSL's IVV were invited to enrol in the study. Study participants were asked to report solicited adverse events (AEs) occurring within seven days after each vaccination and MAEs occurring within seven days after each vaccination, via an internet-based survey.
Setting	This observational research study was implemented through the primary care research network of the National Institute for Health Research (NIHR) in the United Kingdom (UK).
Participants and study size	The source population were individuals who presented to investigator sites for influenza vaccination, either through mass vaccination clinics or opportunistic vaccination during routine consultations, and who received bioCSL's IVV. This observational post-marketing study was designed to capture the population receiving bioCSL's IVV regardless of age or health status in order to provide a picture of the safety profile in routine practice. Pregnant and immune-compromised participants, and children aged less than five years were not excluded from this study if they were administered bioCSL's IVV as part of routine care, or inadvertently prior to enrolment in the study. The planned enrolment was up to 400 participants, with the target of 100 participants in each age group: five to < nine years, nine to < 18 years, eighteen to < 65 years and ≥ 65 years.
Variables and data sources	Data collection utilised a mix of investigator site data entry and participant (or parent/guardian) self-reported data entry into a web-accessed electronic database meeting applicable observational research, regulatory and data protection standards.

	The types of variables included in the study were: demographics and baseline characteristics; influenza vaccination information; information on other vaccinations received on the same day as or in the 14 days before this year's seasonal influenza vaccine; clinical at-risk indications for complications from influenza; MAEs; and post-vaccination follow-up.
Results	Data for this report were collected between 15 September 2015 and 19 November 2015. During that period, 462 participants were enrolled. Seven participants were enrolled in the five to < nine years group, 78 were enrolled in the nine to < 18 years age group, 200 were enrolled in the 18 to < 65 years age group, and 177 were enrolled in the ≥ 65 years age group. Of the 462 enrolled participants, 57 (12.3%) did not provide post-enrolment safety data and were therefore not included in the safety analyses. The total number of participants included in the safety analyses was 405. Across all age groups, 41.2% (167/405) of participants reported any solicited local reaction; 32.8% (133/405) of participants reported any solicited systemic symptom; and 7.2% (29/405) of participants reported any solicited allergic reaction. No MAEs related to vaccination were reported.
Discussion	Overall, the reactogenicity profile of bioCSL's IVV gathered for this report is consistent with the known safety profile of bioCSL's IVV. There was one serious, but unrelated MAE within seven days following exposure to bioCSL's IVV. This serious, unrelated MAE concerns a male participant who had a fall and suffered severe facial injury on the day of the vaccination. No new safety signal or information due to unexpected frequency, intensity or the nature of events was identified from this active surveillance. Similarly, the active surveillance at the time of this report has not identified any new safety information that has not been identified through ongoing routine post-marketing surveillance since the start of the Northern Hemisphere 2015-16 season.
Marketing authorisation holder (MAH)	bioCSL GmbH Emil-von-Behring-Str.76 35041 Marburg Germany
Name(s) and affiliation(s) of principal investigator(s)	Dr James Larcombe General Practitioner, Harbinson House Surgery, Front Street, Sedgefield Co. Durham, U.K.