Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Laboratory Report

Investigation of Pandemic Vaccine Kit Syringes in relation to a suspected adverse reaction to latex following vaccination

12 October 2009

Background

In October 2009 the TGA undertook testing of 1mL syringes supplied with Pandemic vaccine kits, following a report of a possible anaphylactic reaction to latex after vaccination with the Panvax vaccine in Western Australia.

The manufacturer of the syringes (Steeldrill) has confirmed that the plunger tip is made of natural latex rubber, with a silicone oil coating.

Samples

One box of 1 mL plastic syringes, each contained in a separate sealed labelled plastic bag. No sponsor or manufacturer details were declared on the labelling other than a trademark logo and the statement: Made in China. The following information was provided on the plastic bags:

1mL Sterile/EO Luerslip
Code No. 930100 CE 0123
Mfd Date: 20090315 Expiry Date: 20120315 Lot: 20090315

Testing

Initial testing of the syringes focussed on a comparison by HPLC[1] of the syringes against non-latex containing syringes (Terumo 1mL Tuberculin syringes) when extracted with water or the Pandemic vaccine solution. A latex glove was also extracted with water to act as a control to determine whether peaks unique to the PVK syringe extracts were originating from the latex plunger tip or from other components in the syringes.

The aim of this testing was to determine, firstly, whether there were any gross differences between the syringes and, secondly, whether any visible peaks could be identified as deriving from the latex plunger tip, in particular. This analysis was not expected to provide specific information about the presence of latex protein allergens in the extracts since no reference standards are available in the OLSS laboratories for identification purposes and any such protein would only be expected in nanogram amounts, which is well below the sensitivity of this technique. The following samples were prepared for HPLC analysis:

Sample 1 (+) Latex with vaccine

To each of 10 Pandemic Vaccine Kit (PVK) syringes, 0.1 mL of vaccine was drawn up using a hypodermic needle. The syringes were then inverted to ensure contact between the syringe plunger and vaccine and left for approximately 16 hours. After this time, the vaccine was removed from each of the 10 syringes and combined into a single sample solution of approximately 1 mL.

Sample 2 (-) Latex with vaccine

To each of 10 Terumo Latex Free syringes, 0.1 mL of vaccine was drawn up using a hypodermic needle. The syringes were treated as for sample 1 and the contents then combined into a single sample solution of approximately 1 mL.

[1] High Performance Liquid Chromatography with Photo Diode Array detection

Sample 3 (+) Latex with water

To each of 10 PVK syringes, 0.1 mL of water was drawn up using a hypodermic needle. The syringes were then inverted to ensure contact between the syringe plunger and water and left for approximately 16 hours. After this time, the water was removed from each of the 10 syringes and combined into a single sample solution of approximately 1 mL.

Sample 4 (-) Latex with water

To each of 10 Terumo Latex Free syringes, 0.1 mL of water was drawn up using a hypodermic needle. The syringes were treated as for sample 3 and the contents then combined into a single sample solution of approximately 1 mL.

Sample 5 (+) Latex plungers with vaccine

10 rubber plungers were removed from 10 PVK syringes and placed in a small flask. Approximately 1.5 mL of vaccine was added to the flask, which just covered the plungers. The plungers were left in contact with the vaccine for approximately 16 hours, after which time the vaccine was decanted from the flask and retained.

Sample 6 (+) Latex plungers with water

10 rubber plungers were removed from 10 PVK syringes and placed in a small flask. Approximately 1.5 mL of water was added to the flask, which just covered the plungers. The plungers were left in contact with the water for approximately 16 hours, after which time the water was decanted from the flask and retained.

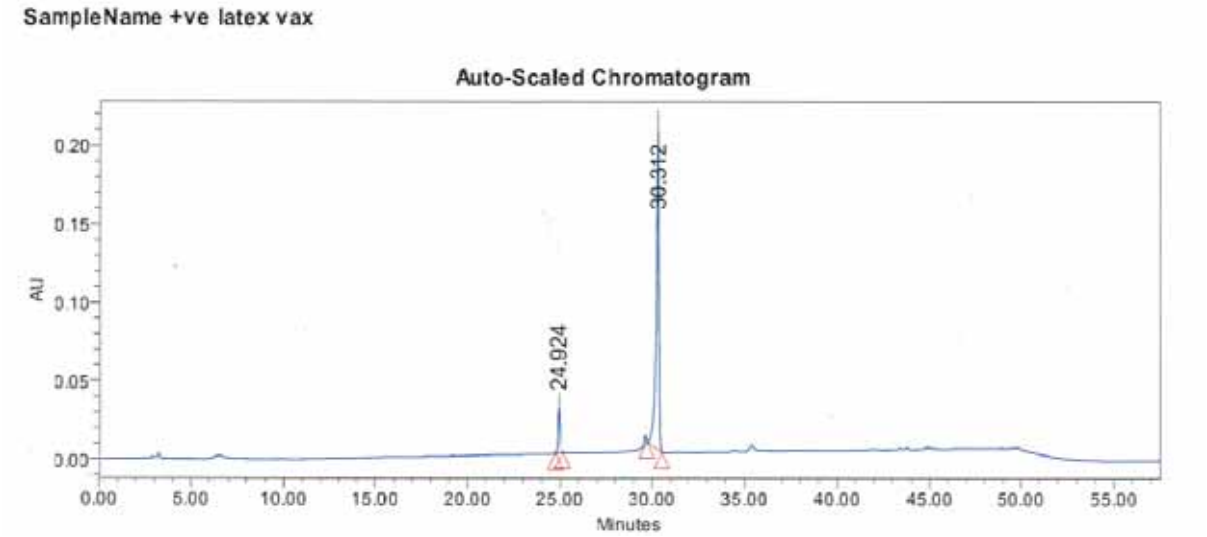
Sample 7 Latex Control

A powder-free latex glove was chopped into pieces and extracted with water for 15 minutes after which time the water was decanted from the flask and retained.

Results

HPLC profiles of the vaccine extracts (Samples 1 and 2) each showed the same 2 major peaks (see **Figure 1** below). The earlier smaller peak has a similar UV profile to aspirin and is probably related to the thiomersal preservative although it does not appear to be thiomersal itself. It may be a hydrolysis product of thiomersal, e.g. thiosalicylate. The second, larger peak is presumed to be due to proteins, which would be consistent with its fairly non-specific UV profile. Both of these peaks originate from the vaccine, not from the syringe.

Figure 1: Vaccine extract of Panvax syringe



The water extracts (Sample 3 and 4) show a number of trace peaks as shown below in **Figure 2**. Note the very low absorption values on the y-axis. A number of the larger peaks are due to column bleed (see blank trace) and do not derive from the samples. The peaks unique to the Panvax syringe are indicated by arrows. The question of whether they are derived from the latex plunger or possibly other components of the syringe (e.g. plasticiser) is partly answered by a comparison against the latex (glove) control (Sample 7) as shown in **Figure 3**.

Figure 2: Water Extracts (Panvax syringe vs Terumo syringe comparator)

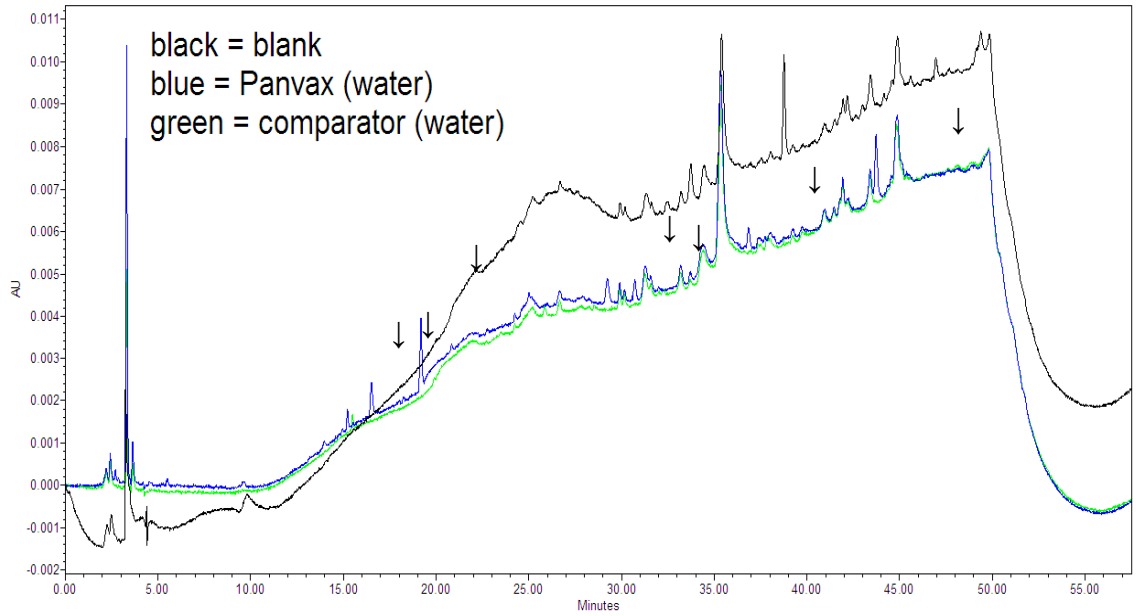
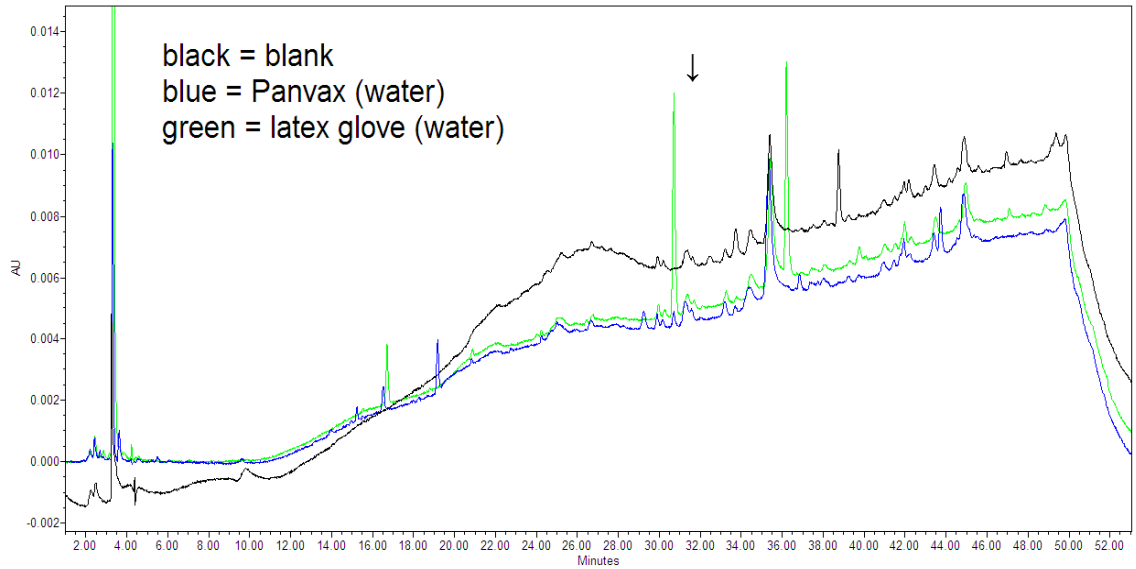


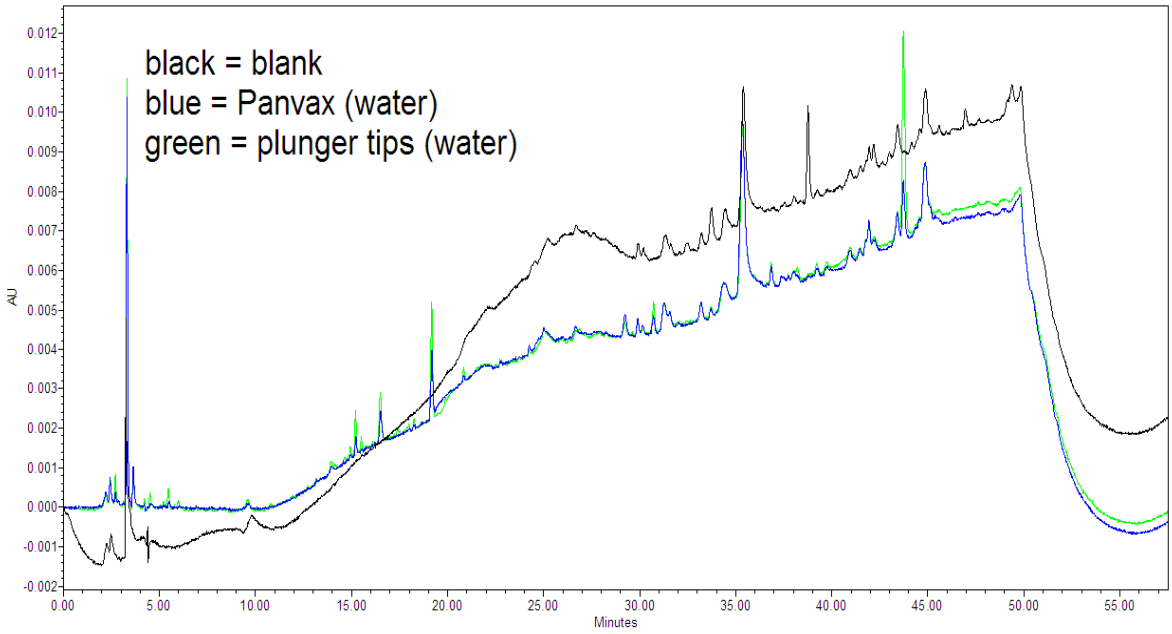
Figure 3: Water Extracts - Panvax syringe vs Latex comparator (glove)



\Of the 7 trace peaks originating from the Panvax syringe potentially only one (see arrow) is common to the latex control based on retention time and UV spectra however the latter is not sufficiently complex to make this an unequivocal match.

Comparison of the water extracts of the Panvax syringes (Sample 3) vs the plunger tips (Sample 6) shows only one peak that is significantly increased in intensity, at a retention time of approximately 45 minutes, as shown below in **Figure 4**.

Figure 4: Water Extracts - Panvax syringe vs Panvax plunger tips



Conclusions

The HPLC analysis of water and vaccine extracts of the Panvax syringes shows that only a few trace organic compounds are extracted from the syringes. Of these peaks, only one minor peak is potentially derived from the latex in the plunger. The main conclusion that can be drawn from this HPLC study is that there are no significant organic contaminants being leached from the latex plunger of the syringe, however given that allergenic proteins would only need to be present in extremely small amounts to elicit an allergic reaction then this testing is not sufficiently sensitive conclusively exclude their presence. Further testing utilising more sensitive methods is recommended.