

28 September 2009

GSK's Pandemrix Vaccine...Let Out Of The Box

By Lara
Health Advocate



GlaxoSmithKline's 'Pandemrix' H1N1 flu virus vaccine has been given a licence for use in Europe by regulatory agencies and the UK is now contracted to buy 60 million doses. This means that in just a few short weeks time the UK population, including babies as young as 6 months and pregnant women, may begin to receive the new vaccine.

The reason the H1N1 vaccine was able to receive such rapid approval is that for the last few years GSK, like many other vaccine manufacturers, have been developing and patenting 'pandemic' flu vaccines.

See Patent [WO2006100109A1](#) to GSK Filed 21st March 2006

“In a preferred embodiment, the influenza strain may be associated with a pandemic outbreak or have the potential to be associated with a pandemic outbreak. In particular, when the vaccine is a multivalent vaccine such as a bivalent or a trivalent vaccine, at least one strain is associated with a pandemic outbreak or has the potential to be associated with a pandemic outbreak. Suitable strains are, but not limited to: H5N1, H9N2, H7N7, H2N2 and H1N1.”

“Example II-Preparation and characterization of the oil in water emulsion and adjuvant formulations. Unless otherwise stated, the oil/water emulsion used in the subsequent examples is composed an organic phase made of 2 oils (alpha-tocopherol and squalene), and an aqueous phase of PBS containing Tween 80 as emulsifying agent. Unless otherwise stated, the oil in water emulsion adjuvant formulations used in the subsequent examples were made comprising the following oil in water emulsion component (final concentrations given): 2.5% squalene (v/v), 2.5% alpha-tocopherol (v/v), 0.9% polyoxyethylene sorbitan monooleate (v/v) (Tween 80), see WO 95/17210. This emulsion, termed ASO3 in the subsequent examples, was prepared as followed as a two-fold concentrate”

GSK actually submitted an application for Marketing Authorisation Approval (MAA) for Pandemrix in February 2007 to the European Medicines Agency (EMA). The application was for a 'mock-up' vaccine containing an H5N1 flu strain. This formulation was granted approval in May 2008. Now, the mock-up flu strain will be

switched to the new pandemic H1N1 strain to produce the current pandemic vaccine. GSK's timing in relation to the 'swine flu' outbreak, as with Baxter, was all but perfect.

Documentation associated with the application and approval can be found on the EMEA web site [HERE](#)

See [CHMP ASSESSMENT REPORT](#)

See [PRODUCT INFORMATION](#)

The documentation details the mock-up vaccine's formulation:

Active Ingredient:

Purified antigen fractions of inactivated split virion

A/Vietnam/1194/2004 NIBRG-14 (H5N1) 3.75 µg HA (mock-up virus)

(NB – this will be switched to A/California/7/2009 (H1N1) v-like strain (X-179A) for the current pandemic vaccine)

Adjuvant:

Squalene 10.68 mg

Alpha-tocopherol 11.86 mg

Polysorbate 80 4.86 mg

Other Ingredients:

Octoxynol 10

Sodium chloride

Disodium phosphate

Potassium dihydrogen phosphate

Potassium chloride

Magnesium chloride

Thiomersal (5µg per dose)

Water for injections

As can be seen from this list, the vaccine contains the organomercury-based preservative 'thiomersal' (also known as thimerosal). In addition, the adjuvant includes the oil 'squalene'. Both of these compounds have been associated with safety concerns, neurodegenerative and autoimmune illnesses. Thiomersal in particular has been removed or reduced in content in many vaccines both in Europe and the USA. Squalene is also a controversial compound, shown by a number of researchers to induce autoimmune disease in animals and has been linked to illness in Gulf War Veterans who were administered the Anthrax vaccine.

None of this is very comforting, and looking more closely at the CHMP documentation submitted to the EMEA, does nothing to inspire confidence in the GSK Pandemrix vaccine.

For instance, the reports detail:

“Safety pharmacology programme... No safety pharmacology studies were performed with Pandemrix vaccine”

“Pharmacodynamic drug interactions...No studies were performed”

“Pharmacokinetics...Experimental studies to demonstrate absorption, distribution, metabolism, and excretion of the active ingredients in Pandemrix have not been performed.”

“Toxicology....There was evidence of an inflammatory response in haematology, clinical chemistry and pathological parameters. Increases in fibrinogen and white blood cell counts were noted in temporal association with the erythema and oedema noted on observing the rabbits. Relative to body weight, the spleen weight was increased in all groups compared to the control (7 - 41%)”

“Frequency and severity of fasciitis was higher in rabbits from the vaccine group. This toxicity was attributed to the adjuvant.”

“Minor changes indicative of an inflammatory response were noted in clinical chemistry and haematology in rabbits dosed with AS03 or with the trivalent influenza vaccine.”

(NB- some of these effect were claimed to be reversible over subsequent weeks, based on testing animals after a longer-time delay)

“Carcinogenicity...No carcinogenicity studies were conducted which is in line with the Note for Guidance on Preclinical pharmacological and toxicological testing of vaccines”

*“Reproduction Toxicity....There was one unexpected death in a maternal rat: however, this was **judged** unrelated to the vaccine”*

“Local tolerance....very slight oedema noted in one rabbit 3 hours after injection of the adjuvant AS03”

In the human trials, adverse events include:

Blood and lymphatic system disorders

Common: lymphadenopathy

Psychiatric disorders

Uncommon: insomnia

Nervous system disorders

Very common: headache

Uncommon: paraesthesia, somnolence, dizziness

Gastrointestinal disorders

Uncommon: gastro-intestinal symptoms (such as diarrhoea, vomiting, abdominal pain, nausea)

Skin and subcutaneous tissue disorders

Common: ecchymosis at the injection site, sweating increased

Uncommon: pruritus, rash

Musculoskeletal and connective tissue disorders

Very common: arthralgia, myalgia

General disorders and administration site conditions

Very common: induration, swelling, pain and redness at the injection site, fever, fatigue

Common: shivering, influenza like illness, injection site reactions (such as warmth, pruritus)

Uncommon: malaise

Mostly the reactions were worse for the sub-groups receiving adjuvanted formulations, and the rates were generally higher in the lower age group band 18-60 c.f. >60. NB the trial did not include anyone under 18 years old and the report details that there is no trial experience in children. This is of concern, as the CHMP report states:

“Pandemrix is commonly or very commonly associated with a range of local and systemic adverse reactions but these are not often of severe intensity and the safety profile would not preclude the use of the vaccine in healthy adults aged 18-60 years or > 60 years”

No trend analysis is provided in smaller age sub-sets i.e. whether there were more reactions in subjects aged 18-25 yrs cf. higher age brackets in the under 60's group. If the trend is for reactions to be worse in line with decreasing age, this does not bode well for administration of the vaccine in babies, infants or adolescents.

Serious adverse events (SAE) were reported by ~30 patients – but these are not detailed, and were none were 'considered' to be related to the vaccination. There is also no data on co-administration of Pandemrix with other vaccines.

It is not clear how well or by what criteria GPs will assess someone to be a 'healthy adult' and therefore covered by the vaccine trial data. Would someone diagnosed with ME/CFS be considered healthy enough for the vaccine? It does not appear that they have been included in the studies, and therefore the adverse effects of the vaccination would be a complete unknown for them. Underlying mitochondrial dysfunction is known to be part of the ME/CFS pathology, and vaccines, as shown for instance in the case of Hannah Poling, can aggravate this problem.

GSK now plans to trial the vaccine in an additional 9,000 patients, but these patients will be monitored for a matter of days or weeks after their shots, so any kind of delayed hypersensitivity or rate of onset of autoimmune or other illness may not be picked up before a mass vaccination campaign begins.

To date there have only been 80 swine-flu related deaths in the UK in 2009 and in general, symptoms are not severe. It really must be considered whether it is safe or appropriate therefore to begin mass vaccinating populations with a fast-tracked vaccine with little or no testing or post-marketing surveillance in the majority of the target population, and especially the under-18's. The only parties who stand to gain significantly from this vaccination programme at present, are the vaccine manufacturers and GPs surgeries who will receive a payment of £5.25 per dose of vaccine administered. Somewhat ironic, when you consider that [33% of nurses](#)

surveyed and a staggering [60% of doctors](#) have said that they would not be vaccinated themselves due to vaccine safety and efficacy concerns.

If it is not good enough for doctors and nurses, based on the mild symptoms, and fears of inadequate vaccine safety and efficacy then why should it be OK for anyone else? But blinded by the money and government dogma, no doubt the vaccines will be administered to millions of people unless they put up their own resistance.

In the end, it will be down to a well-informed public to ensure that H1N1 vaccines such as GSK's Pandemrix, or more aptly 'Pandorix', are not let out of the box.

Lara, Health Advocate

28 September 2009