

## GSK malpractice case raises questions about trial standards

An ongoing legal case between GlaxoSmithKline and courts in Argentina has drawn attention to possible procedural problems in trials done in developing nations. Natalia Fuertes reports.

After GlaxoSmithKline (GSK) was fined US\$92 000 by Argentinian courts for administrative irregularities in a vaccine trial, observers have questioned whether trials are done under the same strict principles all over the world.

On Dec 28, 2011, Marcelo Aguinsky, a judge in the province of Mendoza, found GSK guilty of irregularities in obtaining informed consent in a trial assessing the efficacy and safety of Synflorix—a vaccine against *Streptococcus pneumoniae* and acute otitis media caused by non-typeable *Haemophilus influenzae*. Aguinsky fined the drug company and the two main investigators, Miguel Tregnaghi and Hector Abate, a total of AR\$1 million. GSK is currently appealing the decision. “GSK conducts clinical trials to the same high standards, irrespective of where in the world they are run”, the company said in a statement.

The COMPAS trial was done between 2007 and 2008 in rural areas of three provinces in the east and north of Argentina—Mendoza, Santiago del Estero, and San Juan. It involved around 400 health professionals and was originally intended to recruit 17 000 children.

Problems in the GSK trial first came to light in 2007, when paediatrician Ana Marchese reported possible irregularities to FeSProSa (Syndicate Federation of Argentinian Health Professionals) after speaking to the trial participants’ families. FeSProSa investigated the accusations and filed a report to the National Administration of Drugs, Food and Medical Technology (ANMAT) in December, 2007, declaring problems surrounding informed consent. GSK stated that it was the company that had identified the irregularities through self-monitoring and reported them straight to ANMAT.

ANMAT undertook an inspection of the procedures and consent forms and found that in some of them, there was reason to believe that the parents of the participants did not fully understand what they were signing and the witnesses were not impartial. Due to these irregularities, the recruitment process was stopped in August, 2008. Roberto Lede, director of Planning and Institutional Relationships of ANMAT, states that “the intervention of the ANMAT was very opportune. The recruitment was stopped in the way it was being carried out and resumed with intensive control. It should be noted that the irregularities only affected less than 1% of the subjects.”

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14 infants who were taking part in the COMPAS trial died during it. However, because they were in the placebo group, GSK and ANMAT agreed that the trial could continue. COMPAS ended successfully in 2008, with only 18% fewer subjects than originally intended, and Synflorix was approved by ANMAT.

However, as the problem regarding invalidity of some of the consent forms remained, ANMAT issued a fine to GSK and the local doctors in charge. While GSK are appealing the fine in Mendoza, in Santiago del Estero, their appeal to the Supreme Court was successful, and the ruling was dismissed. In San Juan, the local courts have yet to rule.

The ruling of the Argentinian courts marks a pivotal moment in the regulations of trials by local authorities. Luis Petri, a member of the Lower House in Mendoza presented a bill in

early January, 2012, to ban clinical trials in the province. “Children of Mendoza must not be used as guinea pigs by pharmaceutical companies to try their drugs or vaccines, regardless of the consent of their parents”, he stated. The bill is still under consideration.

In 2007, about 200 trials were done in Argentina, but not all of them were officially registered. After the irregularities in the COMPAS trial were disclosed, the government decided to create a National Register of Trials. In November, 2008, ANMAT ordered drug companies throughout the country to include a warning sign in red capital letters on every consent form, clearly stating the experimental nature of the trial. However, ANMAT’s Lede said that “there was no need to introduce any modifications to the law; the problem was not the law but the compliance with it”.

Brian Angus, director of the Wellcome Trust UK Centre for Clinical Tropical Medicine in Oxford, UK, states that “protection of volunteers for clinical trials is crucial. Especially overseas, where people sometimes do not have the level of education to understand the implications of a clinical trial, there is even greater need for the doctors to act in the patient’s best interests. It is ultimately the doctor’s responsibility. What would you do if somebody agrees to be part of a clinical trial but you do not think they really understand what it means? The answer is clear, you do not recruit them.”

GSK’s fine is the largest Argentina has issued against a drug company. And while the case has led to legal changes in the country, it has also drawn attention to the need to improve ethical and procedural standards of trials done in developing regions of the world.

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