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Response to Serrao and Goodchild

J. R. Sneyd *Faculty of Health*

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CORRESPONDENCE

Response to Serrao and Goodchild

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EditordSerrao and Goodchild1 have correctly identified an author's error2 for which I apologise. The lipid-free presentation of an i.v. anaesthetic is a sensible ambition, and their strategy of formulating alphaxalone in a 7-sulphobutyl ether b-cyclodextrin solution 13% is rational. Their preliminary publications confirm that, in this vehicle, alphaxalone maintains its characteristic of haemodynamic stability whilst being somewhat less lethal to rats than alphaxalone in Cremophor EL 20%.3

I am also hopeful for new i.v. anaesthetics, but enthusiasm has to be grounded against the universal availability of lowpriced generic propofol. To achieve commercial success will require satisfying regulators that the vehicle is safe and persuading anaesthetists that the haemodynamic improvements are important.

Sulphobutyl ether b-cyclodextrin is already used as a vehicle for injectables, but in very different volumes to those required for total i.v. anaesthesia and intensive care sedation. Clinicians often administer medicines outwith their licensed doses and indications, so considering the extremes is appropriate. When alphaxalone formulated as Althesin (alphaxalone 9 mg ml_1 and alphadolone 3 mg ml_1) was used for intensive care unit sedation, the average infusion rate for sedation was 0.079 ml_1 kg_1 h_1, and one patient weighing 55 kg received a total of 4367 ml (79.4 ml kg_1) infused at 0.2339 ml_1 kg h_1.4 At present, the relative potencies of alphaxalone in sulphobutyl ether b-cyclodextrin 13% and Althesin have not been reported. Nevertheless, sulphobutyl

ether b-cyclodextrin 13%, 0.079 ml kg_1 h_1 would present a cyclodextrin dose of 246.5 mg kg_1 day_1. Sulphobutyl ether bcyclodextrin
13%, 79.4 ml kg_1 is a dose of 10 322 mg kg_1.
Renal and hepatic toxicities have been described in rats receiving sulphobutyl ether b-cyclodextrin 3000 mg kg_1 albeit over a shorter period.5
Haemodynamic stability with alphaxalone is certainly superior to propofol6; however, virtually any patient may be safely anaesthetised with propofol in judicious doses. Bell and Goodchild7 have described the safety of i.v. anaesthesia with propofol in a patient with hypertrophic obstructive cardiomyopathy and aortic obstruction.

Declaration of interest

J.R.S. has received honoraria for advice on pharmaceutical development projects from The Medicines Company, Maruishi Pharmaceutical, and Altus Formulation.

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