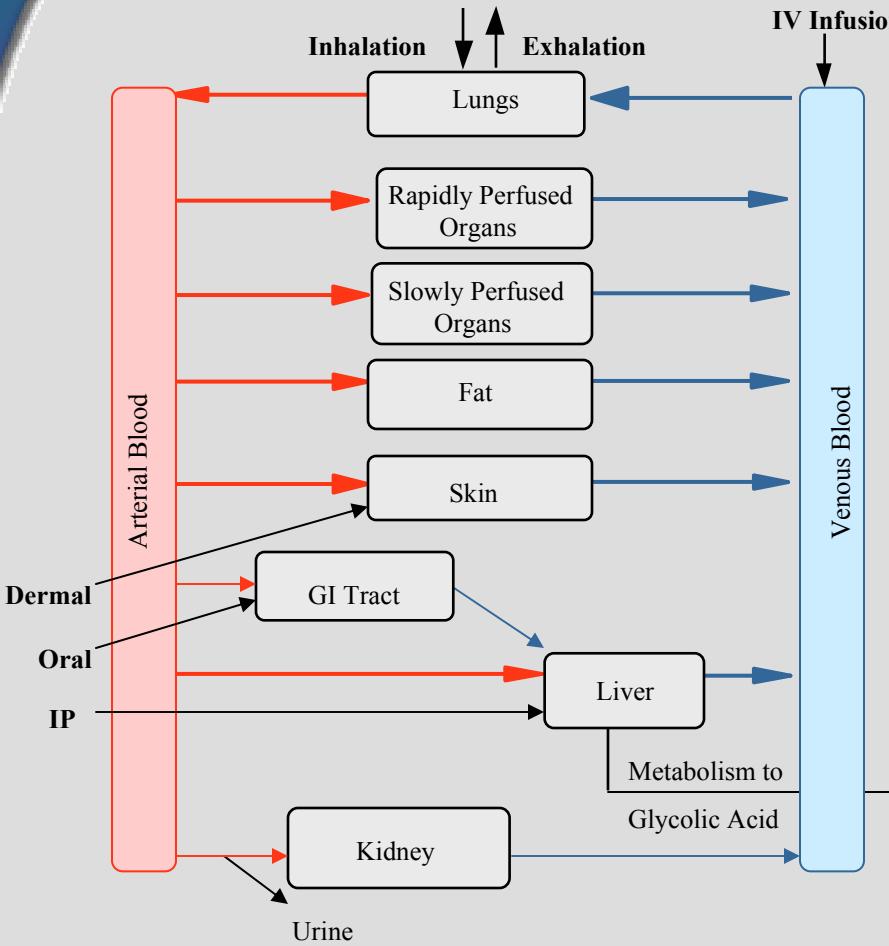


Figure 1. PBPK Model of EG and GA

Male & Female (pregnant & nonpregnant) Rat & Human

Ethylene Glycol



Glycolic Acid

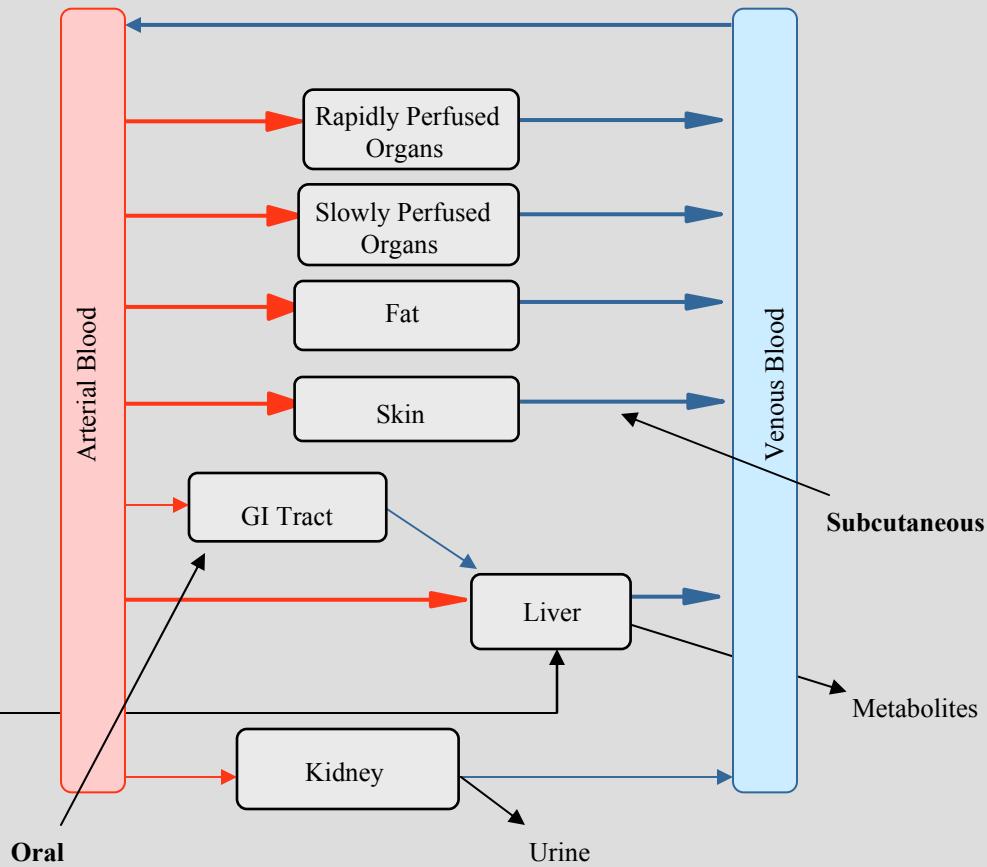


Figure 2. PBPK Model of EG and GA Sources for In Vivo PK Data

SD Rats

- Oral gavage (EG), Male SD Lenk et al., 1989
- Oral gavage (EG), Male SD Hewlett et al., 1989
- Oral gavage (EG), Female SD Sun, 1994
- Oral gavage (EG), Female SD Pottenger et al., 2001
- Oral gavage (EG), Pregnant SD Pottenger et al., 2001
- Oral gavage (EG), Pregnant SD Carney et al., 1997
- Oral gavage (EG, GA), Pregnant SD Carney et al., 1999
- Subcutaneous injection (GA) Pregnant SD Carney et al., 1999
- Oral gavage (EG), Pregnant SD Corley et al., 2002
- Subcutaneous injusion (EG), Pregnant SD Corley et al., 2002

Wistar Rats

- Oral gavage (GA), male Wistar Harris & Richardson, 1980
- IP injection (EG), male Wistar Chou & Richardson, 1978
- Oral gavage (EG, GA), male Wistar Richardson, 1973
- IV injection (EG), male Wistar Weisner, 1986
- Oral gavage (GA), male Wistar Sangeeta et al., 1994

Other Rat Strains

- Oral gavage (EG), male Albino McChesney et al., 1971
- IV injection (EG), male F344 Marshall, 1982
- IV injection (EG), female F344 Marshall, 1982

Humans

- Inhalation (EG), two male volunteers Carstens et al., 2002
- Oral (EG), single male Reif, 1950
- Poisoning Case Reports Numerous

Figure 3. PBPK Model of EG and GA Human PK Data From Poisoning Cases

- | | |
|----------------------|------------------------|
| Baud et al. (1987) | Hewlett et al. (1986) |
| Baud et al. (1988) | Introna et al. (1989) |
| Bowen et al. (1978) | Jacobsen et al. (1988) |
| Brent et al. (1999) | Malmlund et al. (1991) |
| Cheng et al. (1987) | Spillane et al. (1991) |
| Curtin et al. (1992) | Walder & Tyler (1994) |
| Harry et al. (1994) | |

Figure 4. PBPK Simulations of the Kinetics and Renal Clearance of Glycolic Acid

(Ex: Oral dosing of 500 mg/kg GA; all rats 300 g BW vs. 70 kg human female)

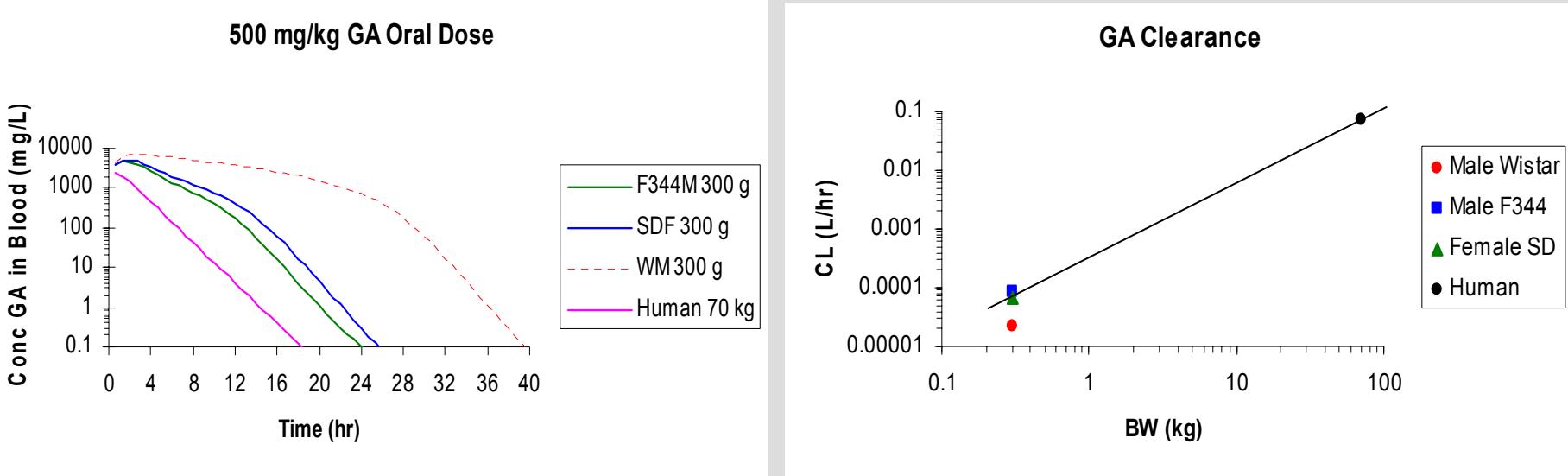


Figure 5. Comparison of Potential Internal Dose Surrogates--Oral (Cmax and AUC for GA in Maternal Blood)

Bolus Oral Dosing of Ethylene Glycol

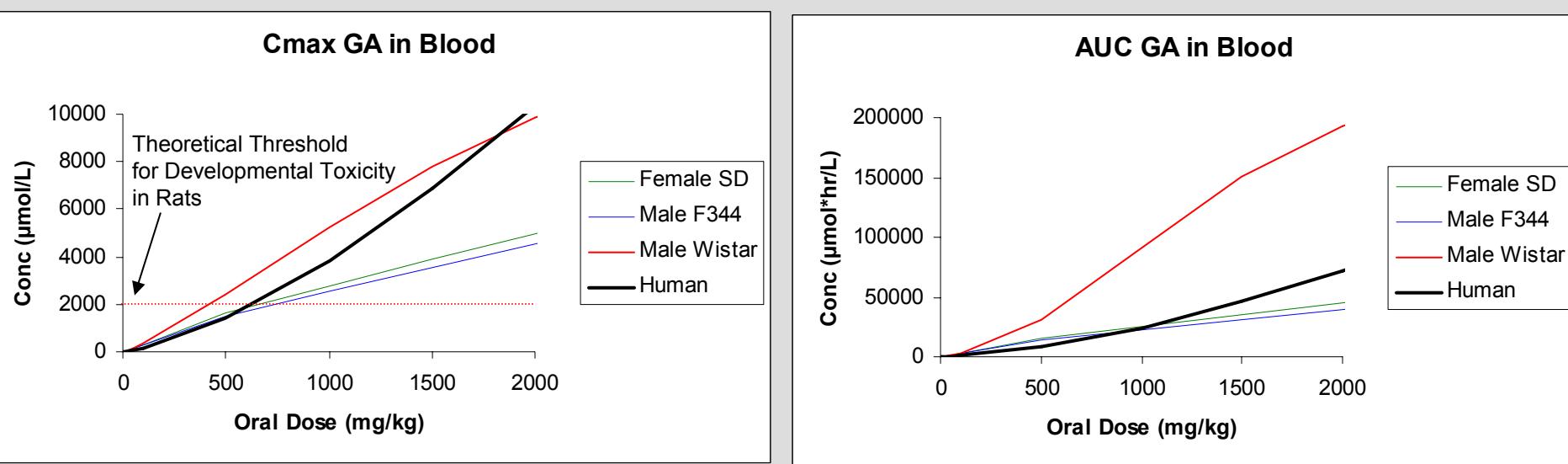
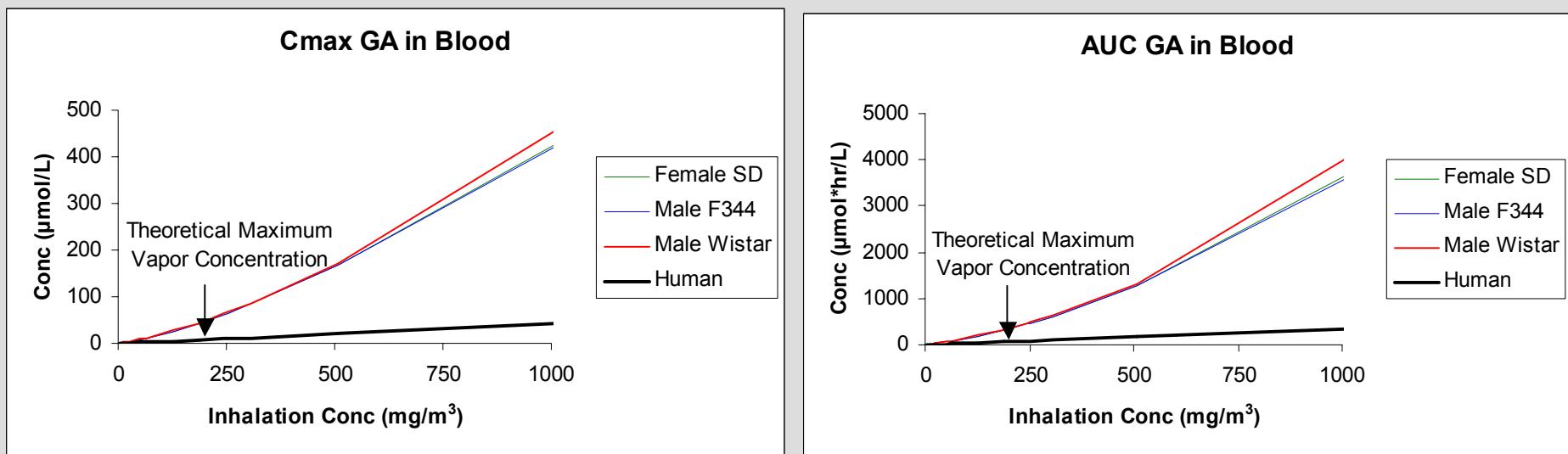


Figure 6. Comparison of Potential Internal Dose Surrogates--Inhalation (Cmax and AUC for GA in Maternal Blood)



Note: Theoretical Saturated Atmosphere at 20C is ~79 ppm (~200 mg/m³) for EG Vapor