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Agilia® SP TIVA TCI Protocols

TCI model constants & input template for TCI model parameters

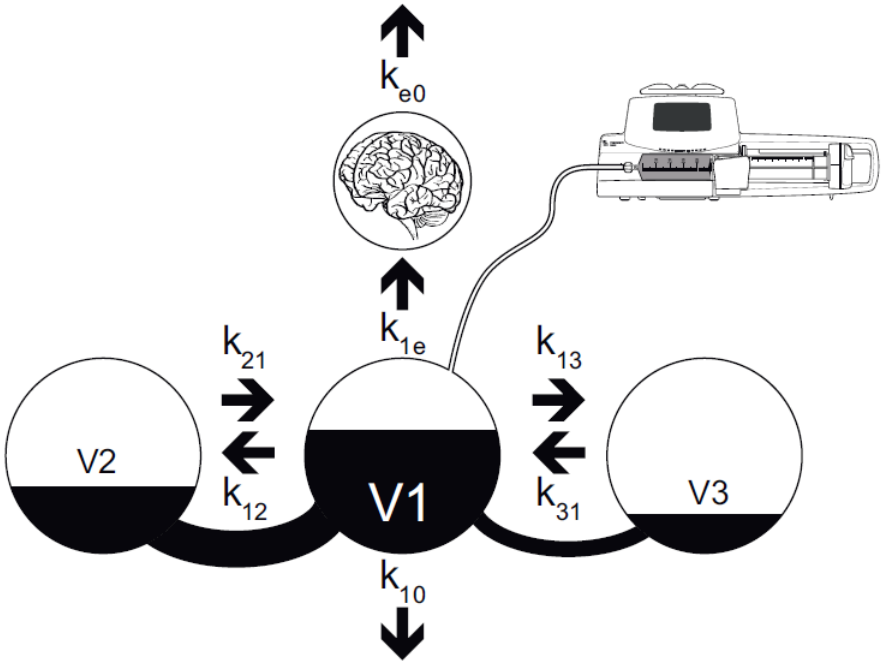
Agilia® SP TIVA

Target Controlled Infusion (TCI)

With TCI programming mode, the pump software must determine the infusion rate pattern required to achieve and maintain a target drug concentration in a body compartment or tissue. The mathematical model used to achieve this concentration is called a pharmacokinetic model.

The pharmacokinetic models included in the pump have already been established and validated through clinical studies whose goal was to assess the model's predictive accuracies in various groups of subjects.

All pharmacokinetic models included in the pump are 3-compartment models that can be represented as follows:



Legend	
V1	Volume of the central compartment (primarily, the blood)
V2	Volume of the fast compartment
V3	Volume of the slow compartment
k_{xx}	The partition coefficients that determine the speed at which the drug travels between
k_{10}	A constant representing the rate of elimination from the central compartment
k_{e0}	A constant representing the equilibrium between the plasma and effect sites

TCI Modes in the Agilia SP TIVA

The pharmacokinetic models included in the Agilia SP TIVA were not developed specifically for the device, but were established and validated by numerous clinical studies.

Be especially careful when using the Marsh and Schnider models for Propofol. These two models lead to different flow rate patterns, and the proper concentration can differ depending on the choice of model.

With TCI programming mode, drugs can be infused according to the target control modes below (TCI modes):

- Plasma Control Mode: control of plasma concentration
- Effect-site Control Mode: control of effect-site concentration

Effect-site control mode differs from plasma control mode by allowing an overshoot of the plasma concentration to rapidly achieve the effect-site concentration. Before using the effect-site control mode, you must evaluate the patient's state of health. Be careful using the effect-site control on fragile (ASA 3 or 4) or elderly patients.

In TCI mode, it is always best to titrate the concentration. This involves finding the proper concentration for your patient by progressively increasing the target until you reach the desired effect.

Age

The TCI modes can be used on patients of ages 1 to 100 however this may be limited in certain models. You must be especially careful with the Marsh model since it does not take age into account. For patients aged 55 and older the Schnider model has proven to be more accurate.

Weight

The TCI modes can be used with patients weighing between 5 and 200kg. For mobidly obese patients, the pharmacokinetic models accuracy has not been validated, and the TCI modes should be used with caution. Additionally, the Schnider model is dependent on Lean Body Mass (LBM), and cannot be selected when the patient parameters give a calculated BMI (Body Mass Index) of more than 42 for male patients and 35 for female patients.

Pharmacokinetic Models

TCI Model *IV Drug*	Vd (L)	k10 (min-1)	k12 (min-1)	k13 (min-1)	k21 (min-1)	k31 (min-1)	ke0 (min-1)
Marsh [a] *Propofol*	0.228 × Weight	0.119	0.112	0.0419	0.055	0.0033	1.21
Schnider [b,c] *Propofol*	4.27	0.443 + 0.0107 × (Weight - 77) - 0.0159 × (LBM - 59) + 0.0062 × (Height - 177)	0.302 - 0.0056 × (Age - 53)	0.196	[1.29 - 0.024 (Age - 53)] / [18.9 - 0.391 (Age - 53)]	0.0035	0.456
Minto [d] *Remifentanil*	5.1 - 0.0201 × (Age - 40) + 0.072 × (LBM - 55)	[2.6 - 0.0162 × (Age - 40) + 0.0191 × (LBM - 55)] / Vd	[2.05 - 0.0301 × (Age - 40)] / Vd	[0.076 - 0.00113 × (Age - 40)] / Vd	[2.05 - 0.0301 × (Age - 40)] / [9.82 - 0.0811 × (Age - 40) × 0.108 × (LBM - 55)]	[0.076 - 0.00113 × (Age - 40)] / 5.42	0.595 - 0.007 × (Age - 40)
Gepts [e] *Sufentanil*	14.3	0.0645	0.1086	0.0229	0.0245	0.0013	0.112
Scott [f,g] *Alfentanil*	2.19	0.0894	0.6540	0.2090	0.1180	0.0177	0.77
Paedfusor [h] *Propofol*	0.458 × Weight * (-0.0576 × Age + 1.1485) × Weight **	0.153 × Weight$^{-0.3}$ + 0.0678 *** 0.0792 **** 0.0954 ***** 0.119 ******	0.114	0.0419	0.055	0.0033	1.21
Kataria [i] *Propofol*	0.52 × Weight	0.066	0.0113	0.051	0.059	0.0032	1.21

a. B.Marsh, M.White, N. Morton, G.N.C. Kenny. Pharmacokinetic model driven infusion of propofol in children. British Journal of Anesthesia. 1991, 67, pp. 41-48.

b. M. M. Struys, et al. Comparison of Plasma Compartment versus two Methods for Effect Compartment-Target Controlled Infusion for Propofol. Anesthesiology. 2000, 92, pp. 399-406.

c. J.H. Seo, et al. Influence of a modified propofol equilibration rate constant (Ke0) on the effect-site concentration at loss and recovery of consciousness with the Marsh model. Anaesthesia, 2013.

d. R.F. Simoni, et al. Clinical Evaluation of two Ke0 in the same pharmacokinetic Propofol Model: Study on Loss and Recovery of Consciousness Review of Brasilian Anesthesiology. 61, 2011, 4, pp. 397- 408.

e. Gepts, Shafer, Camu, Stanski, Woestenborghs, Van Peer, Heykants. Linearity of pharmacokinetics and model estimation of sufentanil. Anesthesiology 1995, 83, pp. 1194-1204.

f. J.C. Scott, K.V. Ponganis, D.R. Stanski. EEG Quantification of narcotic effect: the comparative pharmacodynamics of fentanyl and alfentanil. Anesthesiology, 1985, 62, pp. 234-241.

g. J.C. Scott, D.R. Stanski. Decrease Fentanyl and Alfentanil dose requirements with age. A simultaneous pharmacokinetic and pharmacodynamic evaluation. The Journal of Pharmacology And Expermimental Therapeutics, 1987, N 53855/1 vol.240 n°1.

h. A. Absalom, G. Kenny. 'Paedfusor' pharmacokinetic data set. British Journal of Anesthesia, 2005, 95, 1, p. 110.

i. B.K. Kataria et al. The pharmacokinetics of propofol in children using three different data analysis approaches. Anesthesiology, 1996, 80, 1, pp. 104- 122.

* if patient age < 13 years
** if patient age is between 13 and 16 years
*** if patient age = 13 years
**** if patient age = 14 years
***** if patient age = 15 years
****** if patient age = 16 years

TCI Parameters

Below are the default TCI parameters used throughout Australia in the previous version of the Agilia SP TIVA syringe driver, the Agilia Injectomat TIVA.

On occassion these default settings were modified by customers.

These parameters are provided for your information only and the final parameters chosen for your TCI protocols must reflect your own clinical practice.

Plasma models

		Propofol Marsh Modified (K_{e0} 1.21)	Propofol Schnider	Propofol Kataria	Propofol Paedfusor	Alfentanil Scott	Remifentanil Minto	Sufentanil Gepts
Dilution/Concentration	Dilution 1	10 mg/mL	10 mg/mL	Only available on Agilia SP TIVA syringe driver				
	Dilution 2	20 mg/mL	20 mg/mL					
	N.B either fixed dilutions or range concentrations can be used							
	Range dilution: Minimum			Only available on Agilia SP TIVA syringe driver		50 microg/mL	5 microg/mL	0.5 microg/mL
	Range dilution: Default					100 microg/mL	50 microg/mL	1 microg/mL
	Range dilution: Maximum					500 microg/mL	50 microg/mL	5 microg/mL
Target Plasma Concentration (Cpt)	Hard minimum concentration							
	Soft minimum concentration	0.01 microg/mL	0.01 microg/mL					
	Default concentration	0.1 microg/mL	0.1 microg/mL			0.1 nanog/mL	0.1 nanog/mL	0.01 nanog/mL
	Soft maximum concentration	10 microg/mL	10 microg/mL					
	Hard maximum concentration	15 microg/mL	15 microg/mL			500 nanog/mL	20 nanog/mL	3 nanog/mL
	Wake up concentration	1.5 microg/mL	1.5 microg/mL			50 nanog/mL	1 nanog/mL	0.1 nanog/mL
	Maximum flow rate	1200 mL/hr	1200 mL/hr			1200 mL/hr	1200 mL/hr	1200 mL/hr
Induction	Induction dose: Minimum duration	1 second	1 second			1 second	1 second	1 second
	Induction dose: Default duration	15 seconds	15 seconds			1 second	15 seconds	1 second
	Induction dose: Maximum duration							
Age & Weight	Minimum age (years)	15	15			15	15	15
	Maximum age (years)	100	100			100	100	100
	Minimum weight (kg)	30	30			30	30	30
	Maximum weight (kg)	200	200			200	200	200

Effect-site models

		Propofol Marsh Modified (K_{e0} 1.21)	Propofol Schnider	Alfentanil Scott	Remifentanil Minto	Sufentanil Gepts
Dilution/Concentration	Dilution 1	10 mg/mL	10 mg/mL			
	Dilution 2	20 mg/mL	20 mg/mL			
	N.B either fixed dilutions or range concentrations can be used					
	Range dilution: Minimum			50 microg/mL	5 microg/mL	0.5 microg/mL
	Range dilution: Default			100 microg/mL	50 microg/mL	1 microg/mL
	Range dilution: Maximum			500 microg/mL	50 microg/mL	5 microg/mL
Target Effect-site Concentration (Cet)	Hard minimum concentration					
	Soft minimum concentration	0.01 microg/mL	0.01 microg/mL			
	Default concentration	0.1 microg/mL	0.1 microg/mL	0.1 nanog/mL	0.1 nanog/mL	0.01 nanog/mL
	Soft maximum concentration	10 microg/mL	10 microg/mL			
	Hard maximum concentration	15 microg/mL	15 microg/mL	500 nanog/mL	20 nanog/mL	3 nanog/mL
	Wake up concentration	1.5 microg/mL	1.5 microg/mL	50 nanog/mL	1 nanog/mL	0.1 nanog/mL
	Maximum flow rate	1200 mL/hr	1200 mL/hr	1200 mL/hr	1200 mL/hr	1200 mL/hr
	Maximum Plasma concentration	30 microg/mL	30 microg/mL	1000 nanog/mL	50 nanog/mL	3 nanog/mL
Age & Weight	Minimum age (years)	15	15	15	15	15
	Maximum age (years)	100	100	100	100	100
	Minimum weight (kg)	30	30	30	30	30
	Maximum weight (kg)	200	200	200	200	200

TCI Parameter Input Template

Agilia **Vigilant Master Med DERS**

Agilia SP TIVA TCI Parameter Input Template

TCI Protocol Name	Plasma or Effect-site Model

Therapy Name (optional)

Dilution / concentration: Complete either finite or range

Finite dilution 1		OR	Range dilution: Minimum	
Finite dilution 2 (if required)			Range dilution: Default	
Finite dilution 3 (if required)			Range dilution: Maximum	

Effect-site (Cet) or Plasma concentration (Cpt) targets

Hard minimum concentration	
Soft minimum concentration	
Default concentration	
Soft maximum concentration	
Hard maximum concentration	
Wake up concentration	
Maximum flow rate	

Effect-site TCI protocols only

Maximum Plasma concentration	

Plasma TCI protocols only

Induction dose: Minimum duration	
Induction dose: Default duration	
Induction dose: Maximum duration	

Patient details

Minimum age (years)	
Maximum age (years)	
Minimum weight (kg)	
Maximum weight (kg)	

Authorised Signature	
Name:	
Hospital:	
Date:	
Signature:	

By signing this Agilia SP TIVA TCI input parameter sheet you verify that the parameters chosen have been reviewed and deemed acceptable for clinical use.

Agilia **Vigilant Master Med DERS**

Agilia SP TIVA TCI Parameter Input Template Notes

The available TCI protocols for the Agilia SP TIVA are shown below:

Propofol	Remifentanil	Alfentanil	Sufentanil
Kataria Plasma	Minto Plasma	Scott Plasma	Gepts Plasma
Paedfusor Plasma	Minto Effect	Scott Effect	Gepts Effect
Marsh 1.21 Plasma			
Marsh 1.21 Effect			
Schnider Plasma			
Schnider Effect			

Therapy name: A therapy name is required when there is more than 1 therapy for a drug. The therapy name will not show on the device screen and is used within the Vigilant Master Med DERS to differentiate between multiple therapies of the same TCI protocol. 24 characters max.

Dilution / concentration: Both finite and range dilutions must be expressed as xx dose / xx diluent. e.g 10mg/1mL. Up to 5 finite dilutions can be provided if required. 60mL is max diluent volume.

Target Effect-site, or Plasma, concentration: The required Effect-site, or Plasma, concentration target values must be within the following ranges:

Propofol TCI protocols	0.01 - 15 microg/mL
Remifentanil TCI protocols	0.01 - 20 nanog/mL
Alfentanil TCI protocols	0.01 - 500 nanog/mL
Sufentanil TCI protocols	0.01 - 3 nanog/mL

The above ranges, per drug, also apply to wake up concentration values. The wake up concentration is the estimated drug concentration at which the patient will wake up.

Maximum Plasma concentration: This value is only required for Effect-site TCI protocols and must be within:

Propofol Schnider: 0.01 - 30 microg/mL	Remifentanil Minto: 0.01 - 50 nanog/mL
Propofol Marsh 0.26: 0.01 - 50 microg/mL	Alfentanil Scott: 0.01 - 500 nanog/mL
Propofol Marsh 1.21: 0.01 - 50 microg/mL	Sufentanil Gepts: 0.01- 3 nanog/mL

Induction duration: This value is only required for Plasma TCI protocols and must be within 1 minute - 1 hour.

Maximum flow rate: The allowable flow rate range is between 0.1mL/hr and 1200mL/hr.

Patient age & weight: For any adult TCI protocols the allowable age range is 15 - 100 years and weight range is 30 - 200kg. For paediatric TCI protocols the allowable age range is 1 - 16 years and weight range is 5 - 60kg for Propofol Paedfusor and 3 - 11 years and 15 - 60kg for Propofol Kataria.

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