Supplementary data for Higgins N, Tseng A, Sheehan NL, la Porte CJL. Antiretroviral therapeutic drug monitoring in Canada: current status and recommendations for clinical practice. *Can J Hosp Pharm* 2009;62(6):500-509.

Online Appendix 1. Overview of Existing Antiretroviral Therapeutic Drug Monitoring Services in Quebec and Around the World

Service	Delphic Diagnostics*	Lab Klinische Farmacie†	MUHC‡	Laboratory for Antiviral Research§	Laboratoire de toxicologie et pharmaco-cinétique‖	Malattie Infettive¶
Location	London, UK	Nijmegen, the Netherlands	Montréal, Quebec	University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY	Paris, France	Torino, Italy
Type of service	Clinical (from UK hospitals), research (external studies, many from overseas)	Clinical, research	Primary focus: clinical; secondary goal: retrospective database studies and prospective studies	Multisite clinical research program	Clinical, research	Clinical, research
Drugs measured	PIs, NNRTIs, maraviroc, raltegravir, selected NRTIs	All NRTIs, PIs, NNRTIs, and raltegravir	PIs, NNRTIs	PIs, efavirenz	All drugs, including NRTIs and new drugs (etravirine, maraviroc, raltegravir)	All drugs, including enfuvirtide, etravirine, maraviroc, raltegravir
Consult versus standard of care	Special request according to a matrix of evidence**	Standard of care: provides TDM service to about 10 sites in the Netherlands, caring for about 3000 patients (25% of all HIV-positive patients in the country)	TDM service to about 25 sites in Quebec and to out-of-province sites††	Consult; users must be members of the TDM registry (free); results also added (anonymously) to research database; 26 sites participating	Standard of care, which is well defined in most recent ANRS guidelines, particularly when virologic failure occurs	Testing by special request
Indications	At physician's discretion but generally according to BHIVA guidelines	All indications	Routine testing after initiation of new treatment in patients taking nelfinavir or indinavir and those with multidrug-resistant virus, as well as in cases of virologic failure, toxicity, drug interactions, suspicion of malabsorption, pregnancy, pediatrics, geriatrics, hepatic impairment, once-daily PI therapy, low body weight, unconventional dosing	Virologic failure, suspected drug interaction, food interaction or malabsorption, toxicity, nonadherence with therapy, decreased liver function	Indications consistent with those mentioned in guidelines of most countries, with special mention for drug–drug interactions with new drugs	Drug interactions, cirrhosis, pregnancy, end-stage kidney disease, nonstandard antiretroviral dosing regimens (e.g., unboosted atazanavir, fosamprenavir), unexpected treatment failure, salvage regimens
Type of PK samples	Trough requested but if other samples are sent, an algorithm is used	Random	Trough requested, but random samples accepted in elimination phase, if trough samples not possible; with twice-daily dosing, > 4 h after dose; with once-daily dosing, > 8–12 h after dose	Trough	C_{min} (and C_{max}) for drugs with short half-life, random sampling for drugs with long half-life	C_{trough}, except for mid-dose efavirenz

(continued on page E2)

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Online Appendix 1. Overview of Existing Antiretroviral Therapeutic Drug Monitoring Services in Quebec and Around the World (continued)

Service	Delphic Diagnostics*	Lab Klinische Farmacie†	MUHC‡	Laboratory for Antiviral Research§	Laboratoire de toxicologie et pharmaco-cinétiquell	Malattie Infettive¶
Interpretation guidelines or algorithms	Algorithms, e.g., C_{min}, IQs, concentration ratios; targets generally according to guidelines	C_{min}; random samples extrapolated to C_{min} values using population curves	For PI-naive patients: C_{min} For PI-experienced patients: GIQs (if protease mutations available)	Interpretation that identifies plasma levels as low, expected, or higher than expected relative to literature values	C_{min} guidelines used most often	MECs and GIQs for patients on salvage regimens
Payment agency	35% of UK requests paid by pharmaceutical companies if patient meets specific criteria (e.g., GSK pays for amprenavir testing, Abbott pays for patients receiving lopinavir and amprenavir with or without NNRTI and also pays for all pediatric cases); hospitals fund the other 65% of requests	Government	Ministère de la Santé et des Services Sociaux du Québec	Unrestricted educational grant support from Hoffmann-LaRoche; users responsible for shipping costs	Since February 2005, French national health care service has reimbursed costs of TDM for all antiretroviral drugs	Hospital
No. of samples assessed yearly	4000–5000	5000 (about 100/wk)	1400	No data	25 000	600
Turnaround	Report issued within 2 weeks of receipt of sample	Report issued within 2 weeks	Report issued within 2 weeks of receipt of sample	Report available online within 2 weeks of receipt of sample	Unknown	Unknown

ANRS = Agence nationale de recherche sur le sida, BHIVA = British HIV Association, C_{max} = maximum concentration, C_{min} = minimum concentration, C_{trough} = trough concentration, GIQ = genotypic inhibitory quotient, GSK = GlaxoSmithKline, IQ = inhibitory quotient, MEC = minimum effective concentration, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, PK = pharmacokinetic, TDM = therapeutic drug monitoring.

*For Liverpool Therapeutic Drug Monitoring Service (D J Back, S Khoo, consultants). Website: http://www.delphicdiagnostics.com/

†David Burger, program director. Website: www.tdm-protocollen.nl

‡MUHC = McGill University Health Centre. Laboratory: Royal Victoria Hospital (Denis Thibeault, biochemist); centralized interpretation service: Montreal Chest Institute (Nancy Sheehan, pharmacist).

§Gene Morse, program director. Website: http://tdm.buffalo.edu/

llGilles Peytavin, program director.

¶Affiliated with Ospedale Amedeo di Savoia (Stephano Bonora, program director).

**Matrix of evidence available from: http://www.delphicdiagnostics.com/hiv/products/bioinformatics/

††All HIV patients in Quebec have universal access to a referral service

Online Appendix 2. Data collection form for therapeutic drug monitoring. © 2008 MUHC—Royal Victoria Hospital. Reproduced by permission.

QUEBEC ANTIRETROVIRAL THERAPEUTIC DRUG MONITORING PROGRAM

MUHC – *ROYAL VICTORIA HOSPITAL*
MCR 0277 04-2006

Data collection for blood analysis and clinical interpretation of plasma concentrations

Last name :
First name :
Gender:
Date of Birth :
Medicare #:

Addressograph

Referring Physician: _____ License # : _____

Clinic – Hospital : _____ Telephone # : _____

Mailing address : _____ Fax # : _____

PATIENT INFORMATION:

Weight: _____kg **Height: _____m** ☐ **Pregnancy: If yes, # of weeks gestation: _____**

Race: ☐ **Asian** ☐ **Black** ☐ **Caucasian** ☐ **Hispanic** ☐ **Native** ☐ **Other: _____**

Indication :
- ☐ **Control**
- ☐ **Virologic failure**
- ☐ **Pregnancy**
- ☐ **Hepatic impairment**
- ☐ **Drug interactions**
- ☐ **Pediatrics**
- ☐ **Once-daily dosing**
- ☐ **Toxicity / Adverse drug reactions (specify): _____**
- ☐ **Validation post-dosage adjustment**
- ☐ **Other (specify): _____**

Concomitant medications : _____

Previous virologic failure to protease inhibitors: ☐ **Yes** ☐ **No**

List of cumulative protease mutations OR fax all genotypes to (514) 843-2828:

Adherence: # doses missed over last 48 hours: _____; # doses missed over last 7 days: _____

PROCUREMENT

Date (yy / mm / dd):__/____/__ **Time (00:00) ____ :____**

Test requested for:	Dose (mg)	# doses / day	LAST DOSE Date (yy/mm/dd)	LAST DOSE Time (00:00)	With meal?
☐ Amprenavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Atazanavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Darunavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Delavirdine	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Efavirenz	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Fosamprenavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Indinavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Lopinavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Nelfinavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Nevirapine	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Ritonavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Saquinavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No
☐ Tipranavir	_____	_____	___/___/___	___:___	☐ Yes ☐ No

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REVISION 01-2009