

The Clinton Foundation Pediatric HIV/AIDS Initiative

~Pediatric ARV pricing and quantification~

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- An overview of the Clinton Foundation's Pediatric HIV/AIDS Initiative
- Current Global Pediatric ARV pricing
- A work-in-progress model for forecasting ART needs for children

Clinton Foundation Pediatric HIV/AIDS Initiative

Rationale	Children with HIV have been left behind, yet they are the most vulnerable of all PLHA
Clinton Pediatric ARV Donation	Program launched in April 2005. Donation of 10,000 child-years worth of pediatric HIV formulations to National Treatment programs in 15 high-burden countries worldwide
Program Support	In addition to the drugs, the Foundation provides programmatic support and technical assistance to national programs and selected sites to facilitate scale-up
Long term Strategy	Long term strategy is to change the demand/supply equation for pediatric drugs and make the drugs cheaper for countries to purchase

Current Pediatric ARV Prices – January 2006

Drug	Dose	Formulation	CHAI	CHAI Supplier	Branded	Cipla	Aurobindo
First Line							
Lamivudine*	10mg/ml	Syrup	26.00	Cipla	82.00	58.00	61.00
Nevirapine*	10mg/ml	Syrup	50.00	Cipla	400.00	137.00	411.00
Stavudine*	1mg/ml	Syrup	120.00	Cipla	358.00	153.00	
Zidovudine*	10mg/ml	Syrup	70.00	Cipla	223.00	93.00	
Stavudine*	15mg	Caps	35.00	Cipla			
Stavudine*	20mg	Caps	37.00	Cipla			
Stavudine	30mg	Caps	36.00	Aspen/Cipla/Ranbaxy	48.00	36.00	14.00
Zidovudine	100mg	Caps	153.00	Cipla	241.00		
Zidovudine	300mg	Caps	131.00	Cipla	212.00	131.00	140.00
Nevirapine	200mg	Tab	60.00	Aspen/Cipla/Ranbaxy	438.00	73.00	112.00
Lamivudine	150mg	Tab	59.00	Aspen/Cipla/Ranbaxy	69.00	73.00	66.00
Alternate First Line/Second Line							
Efavirenz*	50mg	Caps	N/A		169.00		
Efavirenz	200mg	Caps	240.00	Ranbaxy	500.00	372.00	438.00
Efavirenz*	30mg/ml	Syrup	N/A		309.00		227.00
Abacavir*	20mg/ml	Syrup	N/A		382.00	292.00	
DDI*	2g	Powder	N/A		133.00		39.00
Lop/r*	80mg/ml	Syrup	N/A		152.00		
NFV*	50mg/g	Powder	N/A		1962.00		
NFV	250mg	Tab	N/A		978.00	1423.00	1533.00

* PPY costs based on a 10kg child

Derived from MSF/CHAI ARV pricing guide

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Future pricing – pediatric FDCs

Company	Name	Drugs	Formulation	Composition	Cost	Comments
Cipla	Pedimmune Baby	D4T/3TC/ NVP	FDC Tab	6/30/50 mg	~90	Commercially available, BE studies completed mid March, PK studies underway in Zambia and Malawi
Cipla	Pedimmune Junior	D4T/3TC/ NVP	FDC Tab	12/60/100mg	~90	
Emcure	Emtri	D4T/3TC/ NVP	FDC syrup	10/40/70mg per 5ml	~120	Available as a powder, needs to be refrigerated once re-constituted, registered in KE, TZ, UG, Zambia Congo, Malawi, Nigeria, Senegal and Ghana. Production factories approved by WHO, PQ pending
Emcure	Emduo	D4T/3TC	FDC syrup	10/40mg per 5ml	~100	

Demand Forecast Model

- No accepted model to determine procurement needs for pediatric patients
- No tool for Industry to obtain forecasting information for production and to guide R&D of new products
- Using inputs from available tools and data, we created a model for ARV demand

Input Variables

- ~ Total children enrollment targets per month or year
- ~ First, alternate and second line regimens and dosing
- ~ Weight distribution of children initiated on treatment
- ~ Formulations (liq vs solid) for each weight class
- ~ Single drug toxicity
- ~ Treatment failure rate
- ~ Buffer stock adjustments
- ~ Pack of bottle sizes (these vary between products)
- ~ Cost of drug with added factors for shipping/clearing

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Input variables: Regimens and Dosing

Recommendations on regimens and dosing taken from:

- **Scaling Up ARV Therapy in Resource-Limited Settings**, *WHO 3 by 5; (2003)*
- **HIV Drug Dose Ranges**, *Harvard AIDS Institute, MSF, ACHAP; (2003)*
- **Pediatric ARV & Cotrimoxazole Dosing**, *CDC, Baylor, Columbia; (2004)*

First Line and alternate First line:

- **AZT+3TC+NVP**
- **AZT+3TC+EFV**
- **D4T+3TC+EFV**
- **D4T+3TC+NVP**

Second Line:

- **ABC, DDI, LPV/r**
- **ABC, DDI, NFV**

Input variables: Regimens

Clinical Assumptions

Treatment Initiation

1st Line Regimen

AZT+3TC+NVP	60.0%
AZT+3TC+EFV	10.0%
D4T+3TC+EFV	5.0%
D4T+3TC+NVP	25.0%

Treatment Failure

2nd Line Regimen

ABC+DDI+NFV	20.0%
ABC+DDI+Lop/Rit	80.0%

The percentage distribution of first line regimens allows for adjustments for national recommendations and the proportion of patients likely to need to be on TB co-treatment

Simple adjustments can be made to change the details the regimens

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Input variables: Weight Distribution

- Used age distribution identified from a UNICEF disease burden model
- Number of children needing ART are the numbers of cases with moderate-severe disease that survive, allowing for time for medical attention to be sought, a diagnosis made, and treatment to be started

Age (y)	Projected Distribution	Weight Band
1	2.4%	3-5 kg
1	4.9%	5-10 kg
2-3	24.7%	10-15 kg
4-5	20.7%	15 - 20 kg
6-7	19.5%	20 - 25 kg
8-9	18.7%	25 - 30 kg
>10	9.1%	30 - 40 kg

Input variables: Weight distribution

Projected Pediatric Patient Weight Distribution

<i>3-5 kg</i>	2.4%
<i>5-10 kg</i>	4.9%
<i>10-15 kg</i>	24.7%
<i>15 - 20 kg</i>	20.7%
<i>20 - 25 kg</i>	19.5%
<i>25 - 30 kg</i>	18.7%
<i>30 - 40 kg</i>	9.1%

Actual Pediatric Patient Weight Distribution

<i>3-5 kg</i>	5%
<i>5-10 kg</i>	10%
<i>10-15 kg</i>	25%
<i>15 - 20 kg</i>	25%
<i>20 - 25 kg</i>	20%
<i>25 - 30 kg</i>	15%
<i>30 - 40 kg</i>	0%

Input Variables

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Input variables: Formulations in weight bands

The split between liquid suspensions vs. caps/tabs are entered for each drug, and based on the weight band dosing, the actual quantity of drug (mls or number of tabs/caps) is calculated for each dose in each weight band

<i>Weight</i>	AZT			3TC		NVP	
	Susp	Caps	Tabs	Susp	Tabs	Susp	Tabs
<i>3-5 kg</i>	<i>100%</i>	<i>0%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>
<i>5-10 kg</i>	<i>100%</i>	<i>0%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>
<i>10-15 kg</i>	<i>50%</i>	<i>50%</i>	<i>0%</i>	<i>80%</i>	<i>20%</i>	<i>50%</i>	<i>50%</i>
<i>15 - 20 kg</i>	<i>20%</i>	<i>80%</i>	<i>0%</i>	<i>20%</i>	<i>80%</i>	<i>20%</i>	<i>80%</i>
<i>20 - 25 kg</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>100%</i>
<i>25 - 30 kg</i>	<i>0%</i>	<i>50%</i>	<i>50%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>100%</i>
<i>30 - 40 kg</i>	<i>0%</i>	<i>50%</i>	<i>50%</i>	<i>0%</i>	<i>100%</i>	<i>0%</i>	<i>100%</i>

Input Variables

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Input variables: Toxicity and Failure

- Model assumes that a certain percentage of patients treated with first line AZT, 3TC, NVP will develop toxicity or failure over the first year of treatment
- Toxicity/Failure estimates based on information derived from partner countries and other programs currently administering ARVs to **adults**
- These numbers are adjustable, and as more accurate data becomes available, toxicity and treatment failure assumptions require adjustment

Toxicity Assumptions	M 2	M 3	M 4	M 5	M 6	M 7	M 8	M 9	M 10	M 11	M 12	
Single Drug Toxicity AZT	2.50%	2.25%	2.00%	1.00%								7.75%
Single Drug Toxicity NVP	1.25%	0.75%	0.50%					0.50%	0.75%	1.00%	1.25%	6.00%
Single Drug Toxicity d4T						0.25%	0.50%	0.75%	1.00%	1.25%	1.50%	5.25%
Failure Assumptions	M 2	M 3	M 4	M 5	M 6	M 7	M 8	M 9	M 10	M 11	M 12	
					1.75%			1.75%				1.75%

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Input: Buffer Stock/Pack Size/Costs

- Buffer stock calculated as additional months of treatment
- Outputs calculated per quarter, so if input is 4 months of buffer stock, an additional month's worth of drugs will be ordered per quarter
- Additional input columns allow you to adjust the pack or bottle size, as well as the costs of drugs and shipping

Outputs:

- # of patients on each drug and formulation during each month
- # of units (ml, caps, tabs) of each drug per month
- # of /boxes/bottles per quarter (with buffer stock)
- Costs per quarter for each drug

Sample Output Page

Drug	Units per Pack	Estimated Cost Per Pack	Import Duties and Freight Costs	Total units per quarter (includes Security Stock)				Total Boxes/Bottles per Quarter (includes Security Stock)				
				Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
				(US\$)	(US\$)							
Suspension												
D4T	200	9.65	10.13	-	-	-	-	-	-	-	-	
3TC	100	2.00	2.20	342,035	340,040	334,090	328,243	3,420	3,400	3,341	3,282	13,444
NVP	100	2.45	2.57	394,207	386,459	379,095	364,910	3,942	3,865	3,791	3,649	15,247
AZT	100	1.53	1.68	481,888	455,404	447,607	445,606	4,819	4,554	4,476	4,456	18,305
DDI	200	14.74	15.48	-	3,699	14,732	25,572	-	18	74	128	220
Lop/Rit	300	41.67	43.75	-	812	3,233	5,613	-	3	11	19	32
ABC	240	31.32	32.89	-	2,889	11,505	19,971	-	12	48	83	143
NFV	7,200	31.17	32.73	-	79,448	316,401	549,208	-	11	44	76	131
Capsules												
D4T (15mg)	60	2.90	3.05	20,355	22,393	21,985	21,069	339	373	366	351	1,430
D4T (20mg)	60	3.00	3.15	28,184	31,006	30,441	29,173	470	517	507	486	1,980
D4T (30mg)	60	3.25	3.58	9,395	10,335	10,147	9,724	157	172	169	162	660
AZT (100 mg)	100	7.00	7.35	155,339	146,802	144,288	143,643	1,553	1,468	1,443	1,436	5,901

The model generates a purchase order



Date
9/27/2005

Re: Purchase Order

Send to:

Bill to:

Clinton HIV/AIDS Initiative
Attn: Jackie Oliveri
225 Water St
Quincy, MA 02169
USA

Product Name	Abbrev	Dosage	Formulation	Pack Size	Quantity	Unit Price US\$	Total Cost US\$
Syrups							
Lamivudine	3TC	50mg/5ml	Solution	100ml	13,444	\$0.91	\$12,234.11
Nevirapine	NVP	50mg/5ml	Solution	100ml	15,247	\$0.93	14,179.43
Zidovudine	AZT	50mg/5ml	Solution	100ml	18,305	\$1.14	20,867.76
Stavudine	d4T	1mg/ml	Solution	200ml	0	\$3.14	0.00
Capsules / Tablets							
Lamivudine	3TC	150mg	Tablets	60	4,533	\$4.91	22,257.85
Nevirapine	NVP	200mg	Tablets	60	4,420	\$5.00	22,102.49
Zidovudine	AZT	100mg	Capsules	100	5,901	\$7.00	41,305.03
Zidovudine	AZT	300mg	Tablets	60	641	\$10.80	6,926.93
Stavudine	d4T	15mg	Capsules	60	1,430	\$2.90	4,147.13
Stavudine	d4T	20mg	Capsules	60	1,980	\$3.00	5,940.19
Stavudine	d4T	30mg	Capsules	60	660	\$3.25	2,145.07
Cotrimoxazole	TMP/SMX	40/200mg/5ml	Solution	60ml	20,183	\$0.21	4,238.37
Cotrimoxazole	TMP/SMX	480mg	Tablets	100	24,714	\$0.70	17,299.48
TOTAL US\$							\$173,643.85

Payment Terms: 30 days upon delivery.

Benefits of The Model

- No similar tool currently exists for pediatric ARV procurement
- Global demand forecast will spur production of low cost – high quality ARV pediatric formulations
- Ordering based on detailed input may help to prevent stock-out and drug wastage
- Quarterly orders allow for readjustments as needed
- Versatility of the model allows for adjustments based on country differences in terms of regimen choice and sequencing
- Over time, as inputs become better defined, the model should become more accurate

Challenges for Model

- There is still not consensus over key issues:
 - Weight band dosing differs from one format to another
 - First and second line regimens are different in different regions
 - Differences over the utility of syrups versus solids. Many advocate using syrups ONLY for infants, and solids for all others.
- Weight to age calculations are estimates and need refinement
- The extent of TB/HIV co-infection is critical for appropriate quantification
- The model is only for children INITIATED on treatment. Does not provide accurate predictions if the population is already treatment experienced
- Strength of model depends on validity of data – regular reporting of usage data will allow for more accurate projections in the future