

Adapting to New International Treatment Standards with Medication Monitors

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The Treatment Dilemma

- Theoretically, strictly administered DOT with Fixed Dose Drug Combinations is the best way to prevent treatment failure and drug resistance.
- In Reality DOT is,
 - 1) Very difficult for many patients, and
 - 2) Universal DOT uses excessive scarce program resources.
- Therefore, after much debate* --->

* Volmink J et. al., Cochrane Database Syst Rev. 2006 Apr 19; (2): CD003343.

WHO No Longer Insists on DOT for All Patients but States

- Clinicians must **assess** adherence and address poor adherence when it occurs.*
- Unfortunately, **assessing** adherence has always been and remains very difficult to achieve

* ISTC The Hague: Tuberculosis Coalition for Technical Assistance, 2006.)

Could Medication Monitors Help Solve the Dilemma?

- Medication Monitors are battery powered portable devices that record when pills are removed from containers.
- Generally thought to be best measure of adherence despite no proof of ingestion.
- Existing Devices are overly expensive

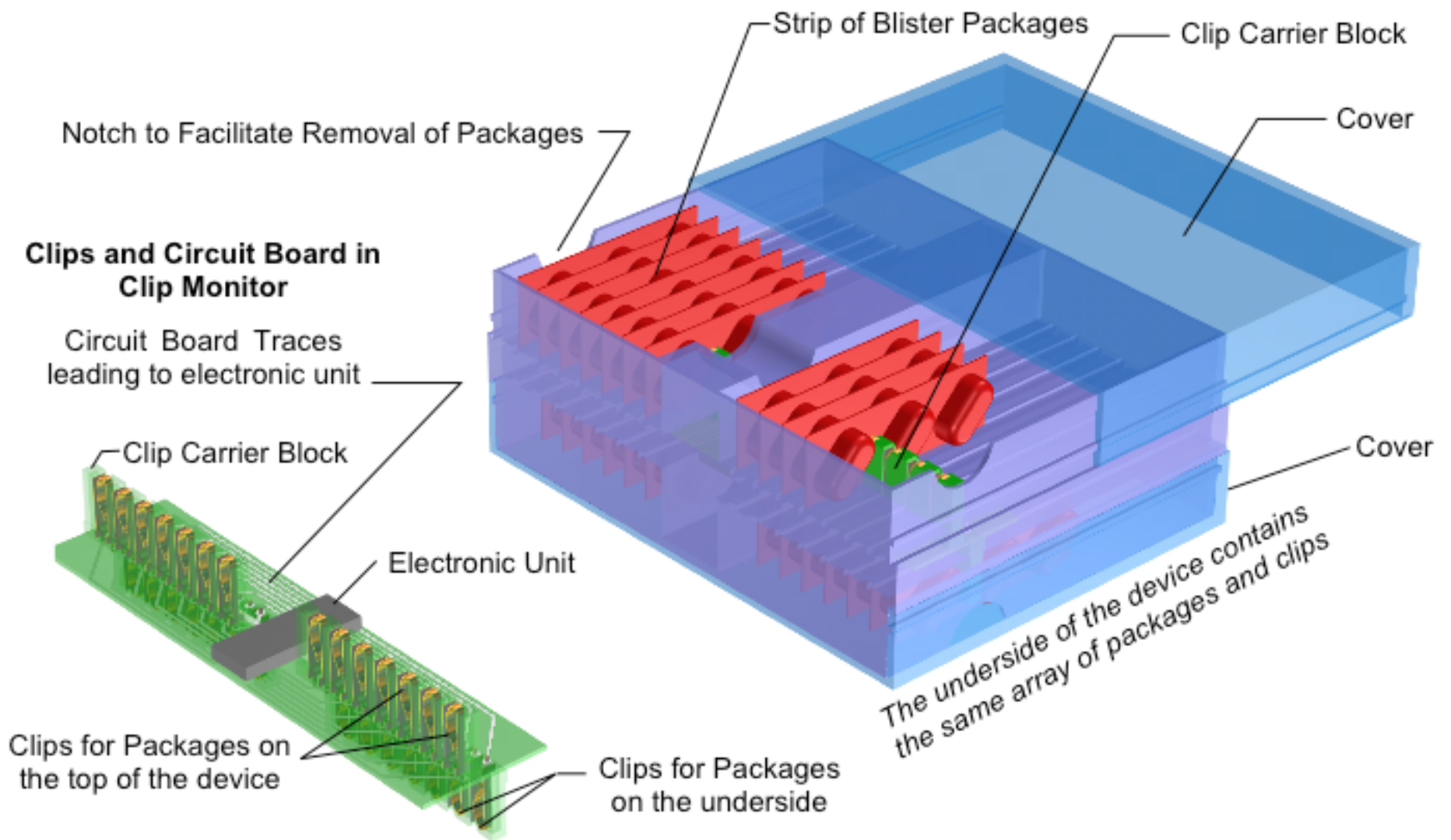
Cost of Mass Produced Medication Monitors

- But modern electronics are very inexpensive.
- Estimated cost to mass-produce a monitor for TB is
- **\$5.00-\$10.00** depending on the design*.
- Per patient costs would be less because device can be re-used for multiple patients.
- By contrast, WHO estimates it costs
**\$26.00/patient for drugs and
\$240.00/patient for all expenditures**.**

Therefore, multiple new devices have been designed and one has been prototyped

* Dr. Danny Hillis - Applied Minds Inc.

** Costs for high burden countries WHO/HTM/TB/2006.362 table19 p 55



Medication Monitor for WHO's Packaged TB Medication

The device determines when strips of blister packages are removed from clips. Two separated flat metallic springs that transmit electricity form each clip. A trace on a circuit board connects each flat spring to an electronic unit. The electronic unit periodically sends electrical pulses to each clip. If a clip holds a strip of packages, the pulse will not be transmitted. If the strip has been removed, the pulse will be transmitted. The time when a pulse is first transmitted is recorded as the time of medication removal. Each strip consists of 2 or more blisters depending on the regimen.

Retrieving Adherence Record with Built in 15¢ LED

- Until now Medication Monitors need PDAs or computers to retrieve the adherence record.
- Unfortunately, PDAs can be lost or stolen, and computers can be “down”.
- However, a built in 15¢ multi-color LED can be used to display the adherence record to
 - 1) Any health care worker or
 - 2) Any community worker in any location.
without computers or PDAs

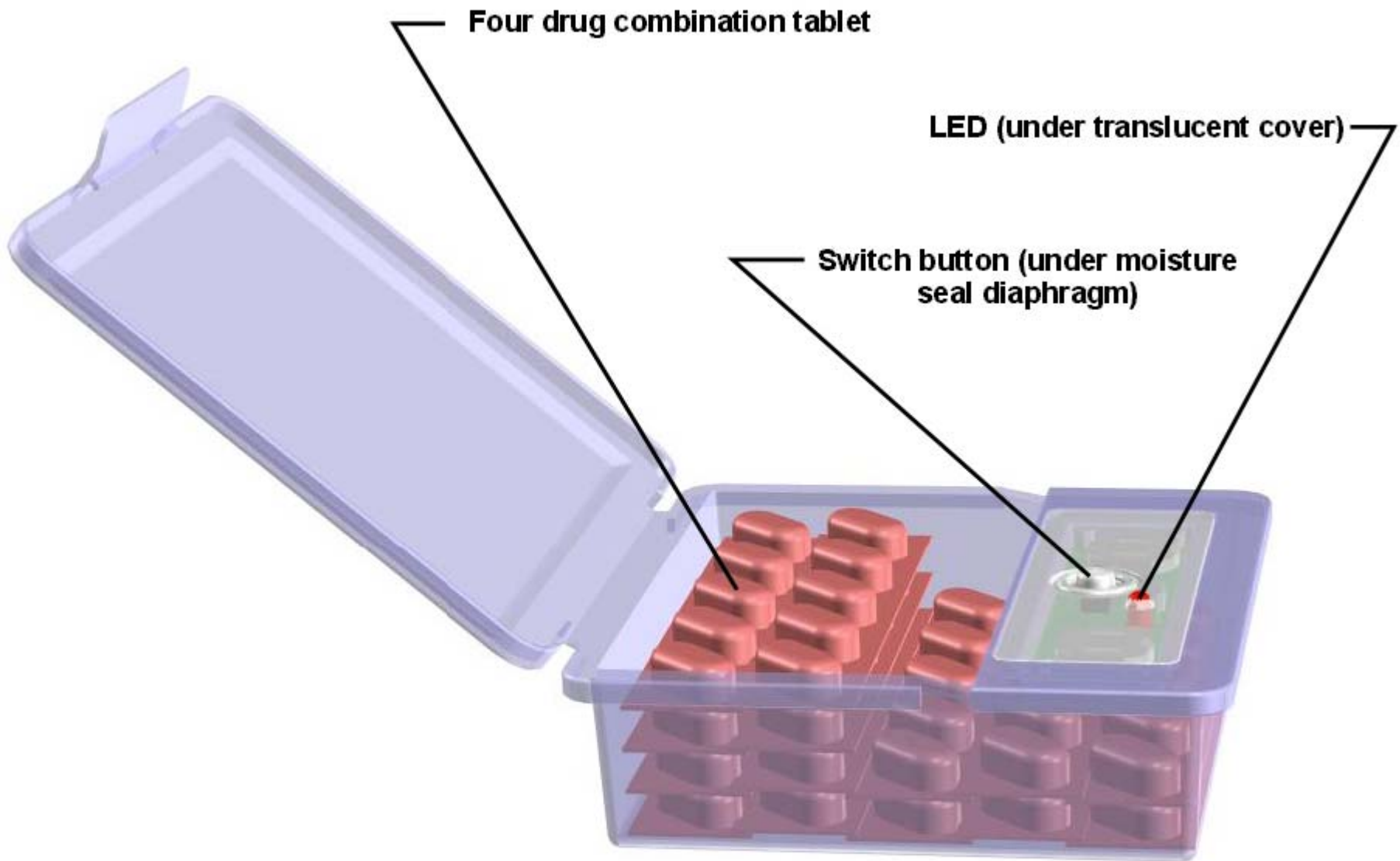


Figure 2: Opened Box Monitor for Global Drug Facility packaged TB medication

Built in LED for Displaying Adherence Record Since Last Refill

With the push of a button the built in LED could show the adherence since last refill with

One green flash for >90% adherence

One yellow flash for 80-89% adherence

Two yellow flashes for 70-89% adherence

One red flash for <70% adherence

Additional red flashes for greater degrees of poor adherence if needed

Built in LED for Displaying Adherence Since Start of Therapy

- With repeated pushes of the button the LED could show the
- total adherence record since the start of therapy

which would be very helpful when managing

1) migrants and patients who move or

3) when the chart is lost.

Built in LED to Assist Patient

- Many patients ask themselves,
“Did I did I not take my pills today?”
- Same 15¢ LED could answer the question.
- When the cover is open
Green flash would say take your pills
Red flash - don't take your pills

Role of Medication Monitors in WHO's Supporter Strategy

- WHO now recommends that all patients have a treatment supporter acceptable to the patient and trained by the health services
who may or may not give DOT*
- If patient is not on DOT, monitors would alert the supporter and authorities to take appropriate action when poor adherence occurs.

* WHO/HTM/STB/2006.37

What Would be Appropriate Action?

- For reliable patients* only monthly refill visits would be needed.
- Less reliable patients could be managed with
 - 1) Additional counseling of patient and family,
 - 2) DOT when needed, and a
 - 3) Longer period of therapy based on the monitor record.

* Zwarenstein et al Lancet 1998;352:1340-43

*) Walley et al Lancet 2001;357: 664-669

Optimal Use of Scarce Trained Human Resources

- Self Administered Treatment (SAT) requires less resources than DOT.
- 60-65% of patients are sufficiently adherent to be successfully treated with SAT in resource limited programs.(1)(2)
- DOT for reliable patients probably wastes resources
- In my opinion adherent patients given SAT are a
- Large Untapped Resource for expanding treatment programs, if identified with medication monitors

1) Zwarenstein et al Lancet 1998;352:1340-43

2) Walley et al Lancet 2001;357: 664-669

Medication Monitors for Private Patients

- Private Physicians treat a large portion of all TB patients.* and usually resist giving DOT.
- Pharmacies or the physicians themselves could give medication in monitors,
- Counsel patients with moderately poor adherence, and
- Refer non-compliers to health authorities for DOT and longer periods of therapy.

*Uplekar Lancet 2001; 358: 912-916

Monitor Supervised Family Member DOT

- Family Member DOT reduces the burden on patients and the delivery system.
- But some say it is a Slippery Slope to Sloppy DOTS.^{*} because you can't trust all family members.
- However, Family Member DOT had higher cure rates than Clinic or Community Worker DOT in recent IUATLD study.^{**}
- Family Member DOT probably improves results somewhat..
- For further improvement medication could be given in monitors with appropriate action for poor adherence &
- **Monitor Supervised Family Member DOT could prove to be the most humane, cost effective, and best form of DOT**

* Frieden T, Sbarbaro JA. Int J Tuberc Lung Dis 2002; 6: 371- 372.

** Thiam et al JAMA 2007 297 380 -386

Collaborators and Website

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Many Evaluators Will be Needed

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Issues to be Evaluated

- Proportion of adherent patients who require minimal attention (only monthly refill visits.
- Effectiveness of counseling based on monitor record in improving adherence
- Effectiveness of extending the duration of therapy when poor adherence occurs
- Proportion of patients who require DOT
- Overall effectiveness of program

Devices for TB Meds #1

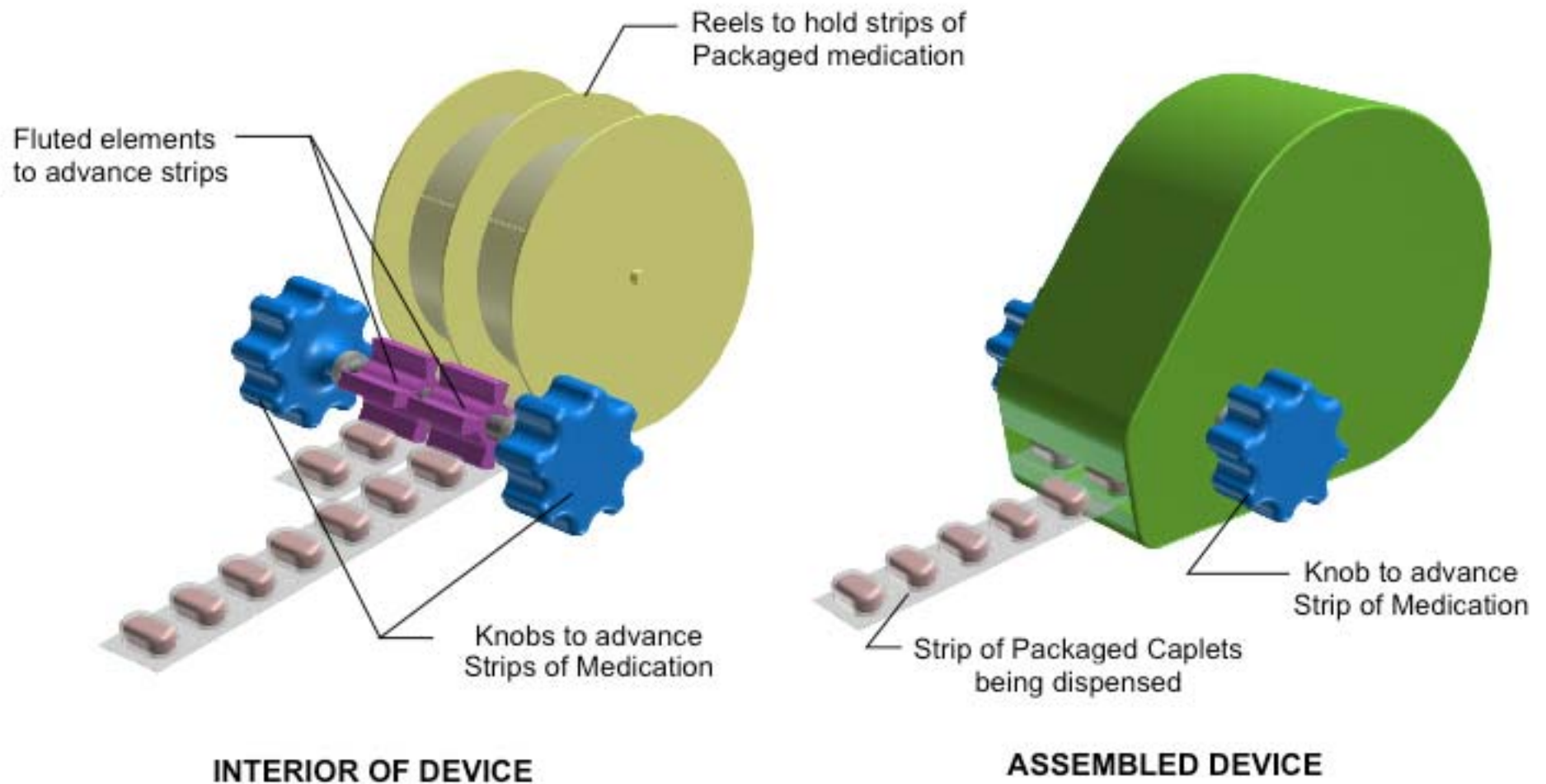
- A device for WHO's Global Drug Facility packaged TB medications has been prototyped.
- It determines when each package is removed from electrically conductive clips.
- Estimated cost when mass produced = \$10.00/device*

* Dr Danny Hillis, Applied Minds Inc. Glendale CA

Device for TB Meds #2

- A device has been designed that determines each time the cover of a medication container is opened.
- Estimated cost/device is less, **\$5.00.**
- Per patient costs would be even less because device can be re-used for multiple patients.
- To put these costs in perspective, WHO estimates for high burden countries it costs
- **\$26.00/patient for drugs and**
- **\$240.00/patient for all expenditures*.**

* WHO/HTM/TB/2006.362 table19 p 55



STRIP PACKAGE MONITOR

The patient is advised how many pills should be taken each day. This dose is obtained by turning a knob, advancing the prescribed number of packages, and tearing off the packages that extend out of the device.

To accommodate a sufficient number of pills for a large person, a second roll of packages with a second knob is available on the opposite side of the device.

Could Monitors Help Reduce Defaulting?

- Avoiding the burden of DOT with monitors should reduce defaulting.
- Two monitor studies found that patients with poor adherence records initially were more like to default. * **
- If patients with poor initial adherence records had
 - 1) Supporter instructed to work more closely with patient
 - 2) Address(s) confirmed, in case patient defaults, and
 - 3) Prompt home visits if a refill visit is missed
 - 4) **There should be less lost patients**

* Moulding TS, Caymittes M. Int J Tuberc Lung Dis. 2002; 6: 313-319.

** Menzies et al Int J Tuberc Lung Dis. 2005; 9: 1343-1348.

How Would Monitor Record Be Used

- For reliable patients* only monthly refill visits would be needed.
- For less reliable patients **appropriate action** would be
 - 1) Additional counseling of patient and family,
 - 2) DOT when needed, and a
 - 3) Longer period of therapy based on the monitor record to compensate for periods of non adherence.

* Zwarenstein et al Lancet 1998;352:1340-43

*) Walley et al Lancet 2001;357: 664-669