**Polymedication Electronic Monitoring System (POEMS) – introducing a new technology as gold standard for compliance measurement**

[§]Isabelle Arnet, Kurt E. Hersberger

Department of Pharmaceutical Sciences, Pharmaceutical Care Research Group, University of Basel, Pharmazentrum, Klingelbergstrasse 50, CH-4056 Switzerland

Authors list

| Full name | Phone number | Fax number | Email address |
|---|---|---|---|
| Isabelle Arnet | + 41 61 267 15 67 | + 41 61 267 14 28 | isabelle.arnet@unibas.ch |
| Kurt E. Hersberger | + 41 61 267 14 26 | + 41 61 267 14 28 | kurt.hersberger@unibas.ch |

§Corresponding author

## Introduction

Non compliance is no longer the simple patient inadequacy to follow the physician's advice. The phenomenon is complex, its occurance is random, his factors are multiple, its predictability is difficult and its public policy implications have been debated over the past decades. Because the knowledge of a patient's medication-taking behavior is a prerequisite for any evaluation of drug effectiveness (1), accurate measurement of compliance gained more and more importance over the years. The ideal measurement of compliance has been described long time ago (2, 3) and should be simultaneously non-invasive, unobtrusive (to avoid the artifact of monitoring a behavior), objective (to produce reproducible data for each subject), practical and cheap (to maximize use and minimize costs); it should yield immediate results and not be open to manipulation.

## From self-report to electronic ink

Traditional indirect measures like self-report, medication diaries, residual pill counting, pharmacy records, clinician opinion (i.e. which do not demonstrate drug ingestion) satisfy many criteria (4). However, they are still limited because of a distant measurement in time and space from the medication-taking event itself. With the emergence of microprocessor technologies in the 1990s, precise timing of medication-taking behavior with oral solid forms could be generated and revealed a comprehensive profile of an individual's drug intake that neither drug serum concentrations nor pill counts would have identified. Although electronic compliance-monitoring devices are considered to provide the most accurate and valuable data (5) and are close to a "gold standard" in measuring adherence, they have been mostly used as a research tool owing to its high costs. Some authors suggest using such devices mainly to educate treatment naïve individuals starting a complex therapy (6).

We present a new technology of electronic adherence measurement of oral solid forms and describe its advantages compared to the electronic devices currently in use.

## Medication Event Monitoring System (MEMS®)

This technology utilizes a computer chip embedded in a specially designed pill-bottle cap to record the time and duration of each opening of the bottle (AARDEX Group Ltd., Sion, Switzerland). MEMS® is today the most sensitive measure of adherence. However, the number of pills taken from the bottle at each opening is unknown and frequently (up to 40% in one study (7)) patients report to have removed pocket doses from MEMS® drug container or having opened bottles without removing drugs for other reasons (8) which may all lead to bias and overestimated adherence (7). This also prohibits the use of MEMS® caps in

conjunction with other adherence support devices, such as pill boxes, where large quantities of pills are withdrawn at one time. Another drawback of MEMS® is that normally only one medication in the regimen can be monitored, therefore only partial adherence is measured.

**Polymedication Electronic Monitoring System (POEMS)**

This novel technology consists of a polymer film with printed electric circuitries (Confrérie Clinique S.A., Lausanne, Switzerland) and allows the recording of date, time and location of drug removal from a blisterpack. This new technology was first developed to fit commercially available standard blisterpacks (9), avoiding the transfer of the pills into a dispenser and keeping the primary packaging intact (Fig. 1a). Multidrug blisterpacks are disposable punch cards like the commercially available easyblist® or Venalink® and contain the different medications in fixed combination to be taken together (so-called “unit-of-use”). The multidrug blisterpacks are filled manually by many community pharmacists in the UK, in Switzerland, Germany or in Australia. Applied on those multidrug blisterpacks (Fig. 2b) the POEMS film allows for remote compliance monitoring of the whole drug regimen, including co-medications. In a recent randomized controlled trial comparing e-blisterpacks and MEMS®-devices, acceptance and internal validity were similar, but the data quality was higher with the e-blisterpacks (10).

Electronic multidrug compliance monitoring has several advantages compared to the MEMS® system. POEMS enables monitoring with one single system in contrast to the filling and handling of multiple MEMS® bottles. Further, the removal of several doses at one time can be recorded as the push through of any single unit-of-use out of the blisterpack will generate an electronic record. Finally, multidrug monitoring provides data with a higher quality (10) leading to a more accurate estimate of adherence.

**Interpretation of patients’ records**

Electronic monitoring of a lead drug with MEMS® device (Fig. 2) is commonly extrapolated to the entire therapy (11), and suspicious records can only be explained by questionning the patient or with the addition of a medication diary (12). However, this procedure defeats the purpose of obtaining purely objective data.

Electronic monitoring of the entire pharmacotherapy with POEMS (Fig. 3) allows the disclosure of distorted intervals. Thus, it helps to distinguish between probable and improbable drug reactions or side effects, and to recognize drug-drug interaction and drug

resistance, since it allows to link the timing of doses with the efficacy of the drug and with critical health incidents. Some pattern like shortening of intake intervalls would remain undiscovered with the monitoring of a lead drug.

## Conclusion

In the search of a gold standard for compliance measurement, electronic films affixed to polymedication blisterpacks seem to fill all the criteria, i.e. non-invasiveness, unobtrusiveness, objectivity, user friendliness. In addition, the transparent compartments on the front side facilitate visual verification of the card content and contribute to the security of drug intake. For the health profesionals, monitoring of the entire pharmacotherapy gives insight into all intake patterns and allows to link desirable and undesirable drug responses to a specific drug. In a close future, one can imagine that medication adherence data can be available simultaneously with breaking the electronic wires, so that a failure to take medication could be detected immediately and intervention could be taken if appropriate.

## Aknowledgments

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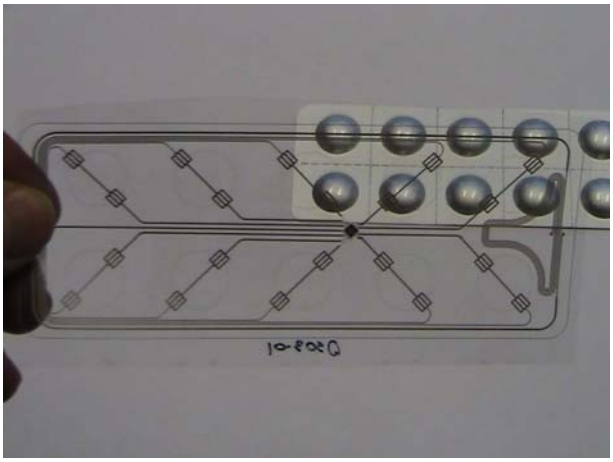


**Figure 1a (left):** electronic foil with conductive tracks, battery and antenna fitting a commercially available blisterpack (Confrérie Clinique S.A., Lausanne, CH.). **Figure 1b (right):** Vinalink® blisterpack (Pharmis GmbH, Beinweil a.S., Switzerland) with conductive loops of electronics on its backside (film side) covering the 7x4 cavities prefilled with patient's individualized medication regimen (front side).

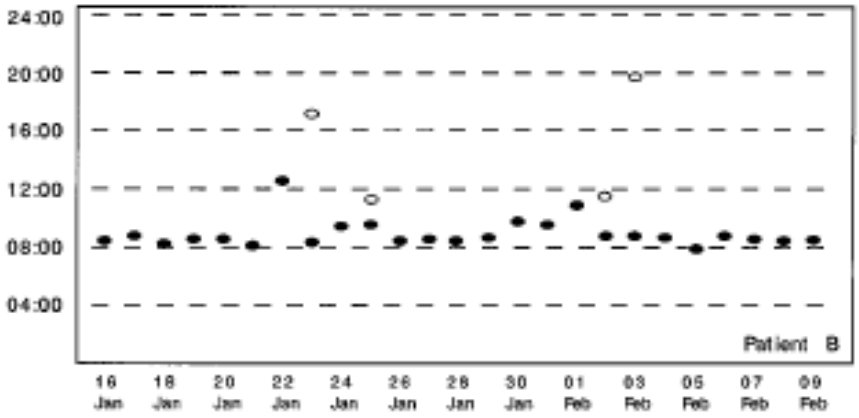


**Figure 2:** Compliance of a once daily regimen recorded with MEMS® device over 3 weeks. Openings with subsequent drug ingestion are depicted as *solid circle*; those without drug ingestion are shown as *open circles*. (8)

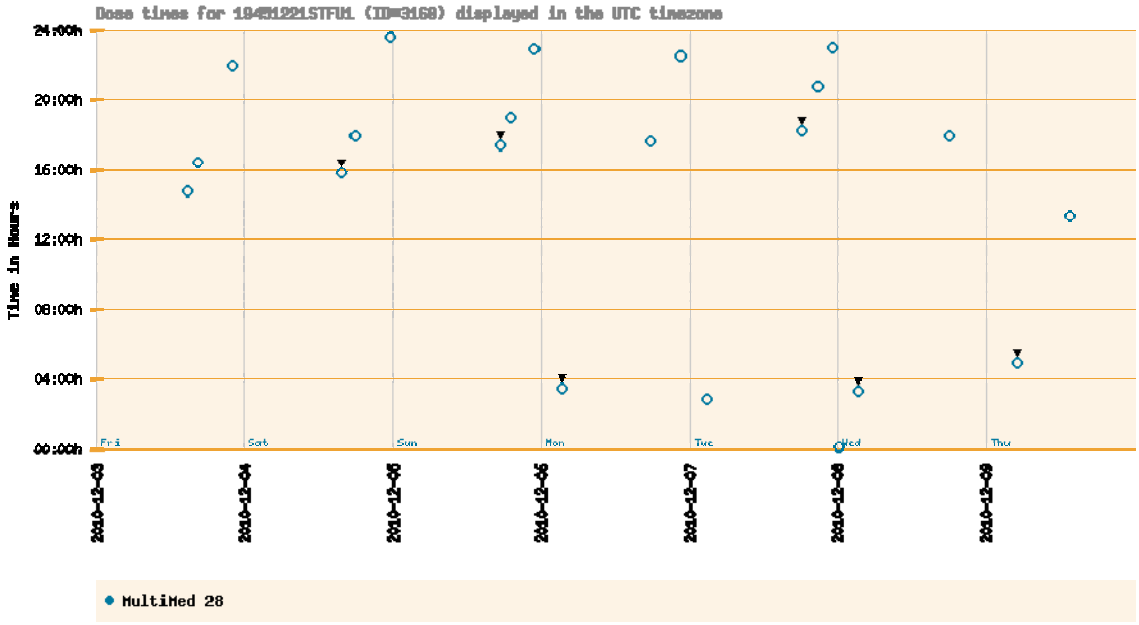


**Figure 3:** Compliance report over 7 days of a thrice-daily regimen using a blisterpack with POEMS. Each circle represents the pushing through of the unit-of-use medication contained in one distinct cavity. The six pills prescribed for the morning were filled in 2 cavities, which had to be opened at the same time. Two pills were filled in the evening cavity and one pill in the bedtime cavity. Triangles depict the breaking of two cavities at the same time.