## Conference Highlight

# Accomplishing Adherence

*Chase Compliance, Pursue Persistence*

**By John Mack**

Lack of adherence—the combined effect of compliance and persistence—is a big problem for the pharmaceutical Industry. In the U.S. alone, the revenue loss due to medication non-adherence is $84 billion. As an example, the per capita spending on diabetes treatment in the U.S. is about $12,000. The majority of that—$7,000—is wasted due to non-adherence.

**Definitions:**

- **Compliance:** % of doses taken as prescribed while patient is actively taking drug
- **Persistence:** number of days from first dose until patient stops taking drug
- **Adherence:** % of doses taken as prescribed for entire period of study (compliance + persistence)
- **Concordance:** physician-patient plan for medications

James Chase, MM&M's Editor-in-Chief, once wrote "To say that tackling patient compliance and persistence poses a challenge to the pharmaceutical industry is like calling Tiger Woods a competent golfer or describing Katrina as a particularly bad storm. It is a gross understate-ment."

But the pharmaceutical industry is getting serious about tackling adherence. A good example of how it is doing this was offered at the recent eyeforpharma Patient Adherence and Persistence Summit, held in Philadelphia, PA.

This article reviews presentations made at the Summit including one by David Baker, VP & General Manager of Shire's attention deficit hyperactivity disorder (ADHD) Business Unit, who presented on "Best Practices for Fostering Adherence."

**Definitions**

No discussion of patient adherence and compliance would be complete without defining a few terms. Baker suggested this definition of Adherence:

**Adherence =**

**Fulfillment + Compliance + Persistence**

where Fulfillment refers to the filling of the very first script for a medication, Compliance means taking the medication as prescribed by the physician, and Persistence refers to the length of time patients take the medication.

**Scope of the Problem**

Why is it important for pharmaceutical marketers to improve adherence?

A World Health Organization (WHO) report—"Adherence to Long-Term Therapies"—estimates that between 30 and 50% of medicines prescribed for long-term illness are not taken as directed. "It is undeniable," says the WHO report, "that many patients experience difficulty in following treatment recommendations."

WHO cites several good health outcomes reasons why it is important to improve adherence (see box, pg. 10). Increased profit for pharmaceutical companies, however, is not on the list. But the promise of getting more profit out of prescription drugs should be a strong incentive for pharmaceutical marketers to get some skin the game, especially when there are fewer new products in the pipeline.

**Adherence in the ADHD Market**

Baker used the ADHD market as a case study. Shire's Adderall XR is indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children aged 6 to 12 years, adolescents aged 13 to 17 years, and in adults. Vyvanse, currently approved for children only, is a new replacement for Adderall XR.

Poor persistence is the main culprit, according to Baker. Persistence with ADHD medication—like most other drugs that do not have a noticeable, immediate effect on lifestyle—is poor. A persistence graph for Adderall over a 10-month period shows that persistence drops from 98% to only 13% (see Figure 1, pg. 10).

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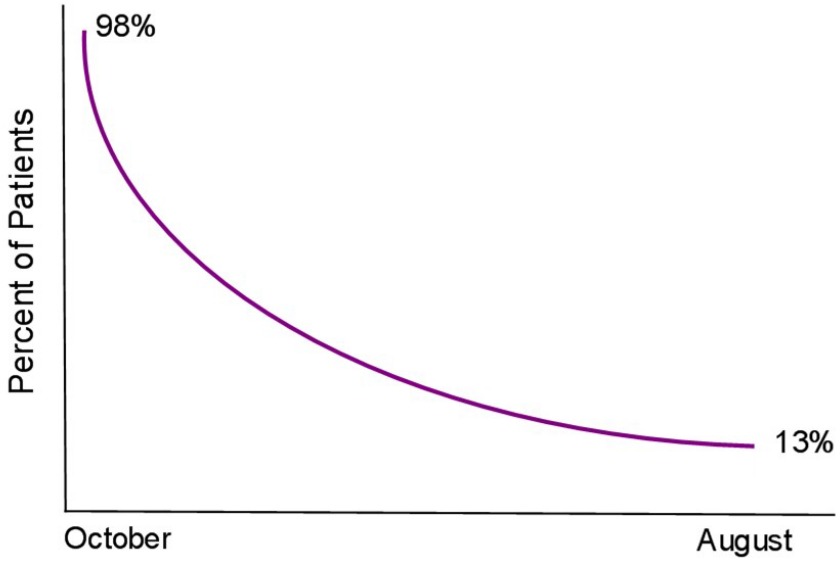


**Figure 1**: ADHD Medication Persistence Over Time.

**Do Your Research**

The drug industry simply does not understand why patients stop taking their medications although there are many theories. What Baker suggested is that marketers must first do the research in their market to find out why their patients are not compliant or why they stop taking their medication.

The ADHD market has its own unique barriers to persistence. Baker described some hypotheses that he believed to be true.

The first barrier is the strong feeling of guilt that parents have about using medication to treat their child's ADHD. Medicine, they feel, is a poor substitute for good parenting. This is probably unique to the ADHD market.

Another barrier is disbelief by the family that ADHD is a medical problem. This might also be a barrier for other medications as well, such as Requip for the treatment of Restless Leg Syndrome.

Some other barriers that Baker enumerated are:

- Media misinformation
- Side effects
- Request for lowest dose that leads to any improvement at all. This may result in suboptimal benefits.

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**A Few of WHO's Adherence Take Home Messages**

- The consequences of poor adherence to long-term therapies are poor health outcomes and increased health care costs
- Improving adherence also enhances patients' safety
- Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments
- Patients need to be supported, not blamed
- Patient-tailored interventions are required
- Adherence is a dynamic process that needs to be followed up
- Health professionals need to be trained in adherence
- Family, community and patients' organizations: a key factor for success in improving adherence
- A multidisciplinary approach towards adherence is needed

The kicker, however, is that ADHD has a strong genetic component and many parents themselves have untreated ADHD. This negatively impacts their child's adherence to treatment.

While these barriers were generally believed to exist in the ADHD market, Shire did some patient/caregiver qualitative research to understand more about the factors that encourage or discourage stimulant medication. Baker emphasized that although the results from Shire's research for the ADHD market may not be applicable to all markets, all brands would benefit by doing a similar study and analysis of their own markets.

Other types of adherence market research include in-office monitoring of patient-physician dialogues, segmentation studies to understand behavioral and attitudinal differences, and making more use of established product relationship marketing programs to recruit patients for market research.

In one particular ADHD research project undertaken by Shire, three groups of parents were interviewed:

- **Continuous Therapy Group**: Parents whose children were on continuous therapy for at least 1 year.
- **Drug Holiday Group**: Parents who medicate their children during the week when they are at school, but on weekends and holidays they would discontinue medication.
- **Discontinued Therapy Group**: Children were on therapy for at least 3 months, then discontinued treatment.

What are the similarities and differences between these groups?

First, the similarities among all groups:

- Poor school performance drove the caregiver to seek treatment in the first place.
- All received minimal information from the prescribing physician.
- Parents reported some form of "relief" in having an explanation for poor performance and having some plan of action for moving forward.
- Parents were concerned about long-term safety and changes in child's personality.

In terms of persistence, it's more important to understand the differences in the three patient groups than the similarities. See Table 1 for a summary of these differences.

"These results were very important to us in order to understand how to communicate to and influence these groups to improve adherence," said Baker.

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| Difference | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| **Initial Concerns** | Resolved | Moderately Resolved | Unresolved |
| **Dosing recommended by physician** | Daily | Only during school | As needed |
| **Description of primary medication benefit** | School and social settings | School only | School only |
| **General attitude toward medication** | Accepting | Not accepting | Not accepting |
| **Parent's self-image** | Courageous, action oriented, trusting | Felt selfish, could do a better job as parent | "Forced" because of lack of other options |

**Table 1**: Differences in ADHD Patient Groups. Group 1 = Continuous Therapy Group; Group 2 = Drug Holiday Group; Group 3: Discontinued Therapy Group.

**Focus on the Patient**
Once the research is done, the adherence program must be developed. As in any marketing program, it is important to decide who is the primary target audience for your adherence messages.

In terms of Shire's solution, Baker explained why Shire focused on the patient/caregiver in its effort to improve adherence. It seems obvious—the patient is the one that exhibits the behavior. However, some people also lay the blame on the physician. According to a study of patient behavior reported in the June 2006 issue of MM&M, seventy-two percent of all patients who stopped taking their drugs lack confidence in their healthcare provider.

But Shire also had these reasons for focusing on the patient:

- better control of the message
- consumers are more willing to listen to 3rd parties about ADHD treatment

Baker didn't get into the role of 3rd parties such as celebrities in adherence messaging, but he did point out that the more control you have over the message, the lower will be your credibility. Shire felt, however, that their communications were very well received by ADHD patients who are thirsty for information.

The messages that Shire thought had the best chance of improving persistence were:

- messages about ADHD and benefits from treatment,
- messages about the product (Vyvanse), and
- messages about how to get the most out of treatment (eg, SHINE program; Figure 2).

**Shire's Solution**
Shire's strategic approach was to ensure that their direct-to-patient (DTP) adherence communications complemented the DTC advertising and approach different patient/caregiver segments—eg., new to therapy, switched from another product, etc.—in different ways, whether it's messaging, tools, frequency, or timing of messages.

"Don't overbuild the program," warns Baker. A program that may work for a small patient segment may not be scalable or affordable for the entire patient population.

**Adherence Tools**
Regarding tools, Baker emphasized the importance of the Vyvanse Starter Kit, which fills in some of the information gaps and helps set expectations. Being upfront about dosing and side effects is critical for improving adherence.

Baker described Shire's SHINE program for ADHD support. Some of the features of SHINE, according the Vyvanse web site, include:

- Tips to improve focus, organization and behavior in your child
- Suggestions for working with your child's teachers
- Vyvanse Success Tracker
- Ideas for building and coaching your child's support team

It also includes multiple mailings—especially during the first few months of treatment—timed to key dropoff points. These mailings are customized according to the age of the patient, whether the patient was switched from another medication or is new to ADHD treatment, etc.

**Forget Forgetfulness?**
"Forget forgetfulness" as a factor in adherence was one of Baker's main take-away points. Reminder programs alone have very little impact on

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**Figure 2**: Vyvanse SHINE Registration Screen.

adherence. Also, although Shire based a lot of its persistence messaging strategy on patient interviews, Baker warned attendees not to rely solely on what patients say are their reasons for non-persistence or non-compliance.

Yet, forgetfulness may be an important issue as more and more consumers take more than one medication per day, some requiring complex dosing regimens. In these cases, reminders may be necessary and technology may help (see, for example, the box about the MedSignals® communicating pillbox).

**Final Tips**

"It takes a lot to move the rock in this area," warned Baker. He was confident, however, that the following "tips" can help in any therapeutic category:

- Use a common language; speak to your consumers in their language from their perspective.
- Understand the data for your market; know your persistence curve! "It's readily available from a number of sources (eg, Verispan)."
- Decide which adherence behavior you want most to influence and improve; is it filling the first script? Is it compliance with therapy as directed by the physician? Or is it persistence?
- Understand the reasons for the behavior that cuts across all conditions, but also understand the reasons unique to your market.
- Decide who to target.
- Design and implement interventions—think messages first, programs second.
- Keep trying!

**Reward Them—Intermittently—and They Shall Adhere!**

Murat Kalayoglu, Director at HealthHonors, talked about "Crafting an Rx Adherence Program with Dynamic Intermittent Rewards" at the conference. HealthHonors describes itself as a consortium that invented a simple solution for the complex problem of medication adherence.

Kalayoglu unequivocally stated that pharma's attempts to improve adherence was a "frustrating, fruitless effort." These include the following tactics:

- Reminder calls
- Alarms
- Calendars

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**MedSignals® Communicating Pillbox**


Adherence is the Achilles Heel of drug efficacy. Without knowing a patient's true compliance, the physician has only the drug to blame when treatments fail.

A new communicating pillbox holds promise for ending the guessing game about drug adherence. The 4-drug portable MedSignals® aids patients in remembering at pill time, records timing of lid openings, uploads usage data daily to host servers, and then reveals adherence patterns to authorized caregivers keeping an eye on patient charts on the web. MedSignals® is the first consumer-priced med-minder with robust communications capability.

Four pill compartments comprise the pocket-size device. Device settings can also be programmed online, enabling caregivers to change settings from their own computers at a distance. At home, the device rests in a cradle connected to phone lines, automatically uploading usage data to the host server every day.

Several signals alert when it's time for any of the four drugs to be taken. Voice announcements (in English or Spanish) remind patients not only how many of each pill to take, but also any instructions associated with the drug. Website "smart charts" depict individual patterns for loved ones or physicians monitoring patients, and aggregate reports identify problems early within a large population for remote case managers.

Funded by six NIH grants for development and clinical testing, MedSignals® consistently demonstrated 13-25% higher adherence rates and high usability scores among low-tech patients. The portable 4-drug model is the first in the product family that is funded by Institutes and in development, many of which will be co-branded, company management says.

According to HealthHonors, all attempts to solve the adherence problem have been "complex, labor-intensive, and overall minimally effective." And if they are effective, they are not scalable to work for all patients. "What is needed is a simple, inexpensive and scalable technology that will be used by patients and embraced by physicians, payors, pharmacies and pharmaceutical companies alike. Something that can be tailored to the needs of each and every patient."

HealthHonors solution is based on rewarding behavior change, a concept that goes back to the studies of B.F. Skinner, the psychologist who invented the "operant conditioning chamber," which is also known as the Skinner Box. The classic Skinner Box experiment uses a pigeon, which gets rewarded with a food pellet every time it pecks the desired key (see Figure 3).

**Figure 3**: Classic Skinner Box with Pigeon Subject.

**Rewards = Behavior Change**

"Rewards work," says Kalayoglu. HealthHonors encourages patients enrolled in its program to call an 800 number when they take their medication to earn points, which can be traded in for real life healthy goodies like discounts at Boscov's, etc.

But patients are NOT rewarded every time they take their medication. A continuous reinforcement schedule in which each specified response is reinforced encourages subjects to think they are entitled to a reward no matter what. Instead, HealthHonors disperses rewards "intermittently"—only some responses are reinforced. Intermittent rewards sustain target behavior over time whereas continuous rewards show a dropoff in target behavior.

Here's how it works. Each time the patient takes the medication, he or she calls an 1-800 number and punches in an identifying code. In a recorded response lasting no longer than 15 seconds, the patient gets a thank you message, a brief educational message, and an indication of points earned.

Perhaps more important is the fact that giving fewer, intermittent awards is cheaper! This is an important consideration when scaling up an adherence program to cover all patients, not just a small subset.

**Pharma Marketing News**

**Patient Compliance: The Problem with Today's Solutions**

Solutions for non-compliance need to focus on a basic rule of human behavior. Put yourself in the mind of the patient and ask "What's in it for me?" Since the benefits of medication compliance are remote and difficult to envision, patients usually make decisions that favor short-term convenience. When you think about it, most of the current methods to boost adherence are actually unpleasant stimuli: alarms, facts to learn, and uncompensated surveys are nobody's idea of fun.

So how can we develop a medication compliance solution that actually works? Behavioral scientists would say that it's obvious: when you want somebody to perform a behavior, your pair it with a positive stimulus. A nebulous stimulus, like "a 7% reduction in your risk of a heart attack," won't work. Are there ways we can provide a definitive, positive stimulus each time patients use their medication properly? That's a question for another day.

--HealthHonors Blog

## Experts Consulted

The following experts were consulted in the preparation of articles for this issue.

- **Vesta Brue**, Chairman/Founder, LIFETECHniques, Inc. (MedSignals®), www.MedSignals.com, 210-222-2067, vesta@medsignals.com
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- **Manuel Prado**, CEO, datumRx, 415-462-2845, manuel.prado@datumrx.com

## Resources

The following resources were used in the preparation of articles for this issue.


- "**Managing the Risks and Regulatory Issues Associated with Successful Pharmaceutical Social Media Monitoring and Marketing**"; http://www.cymfony.com/pharma.asp
- World Health Organization (WHO) report: "**Adherence to Long-Term Therapies**"; http://www.emro.who.int/ncd/Publications/adherence_report.pdf
- "Guidance for Industry: **Postmarketing Adverse Experience Reporting for Human Drug and Licensed Biological Products -- Clarification of What to Report**"; http://www.fda.gov/medwatch/report/guide2.htm



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