

Methylphenidate Regulatory History

**Pediatric Advisory Committee Meeting
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Products**



Approved Medical Treatment Modalities

- Stimulants
 - Methylphenidate Products
 - Amphetamine Products
- Pemoline
- Atomoxetine

Methylphenidate and ADHD over time

- NDA 10-187 Ritalin Tablets (methylphenidate HCl) December 5, 1955 “Minimal Brain Dysfunction”
- 1962 Congress amended the Food Drug & Cosmetic Act to require that a drug demonstrate effectiveness prior to its approval

Formulation Changes

- Extended Release
 - 18-029 Ritalin SR (methylphenidate HCL) Sustained-Release Tablets 3/30/1982
 - 21-121 Concerta (methylphenidate HCL) Extended-Release Tablets 8/11/2000
21-259 Metadate CD (methylphenidate HCL) Extended-Release Capsules 4/3/2001
 - 21-284 Ritalin LA (methylphenidate HCL) Extended-Release Capsules 6/5/2002
 - 21-802 Focalin XR (dex-methylphenidate) Extended Release Capsules 5/26/ 2005

Formulation Changes

- Solutions
 - 21-419 Methylin (methylphenidate HCL) Oral Solution 12/19/2002
- Chewable Tablets
 - 21-475 Methylin (methylphenidate HCL) Chewable Tablets 4/15/2003

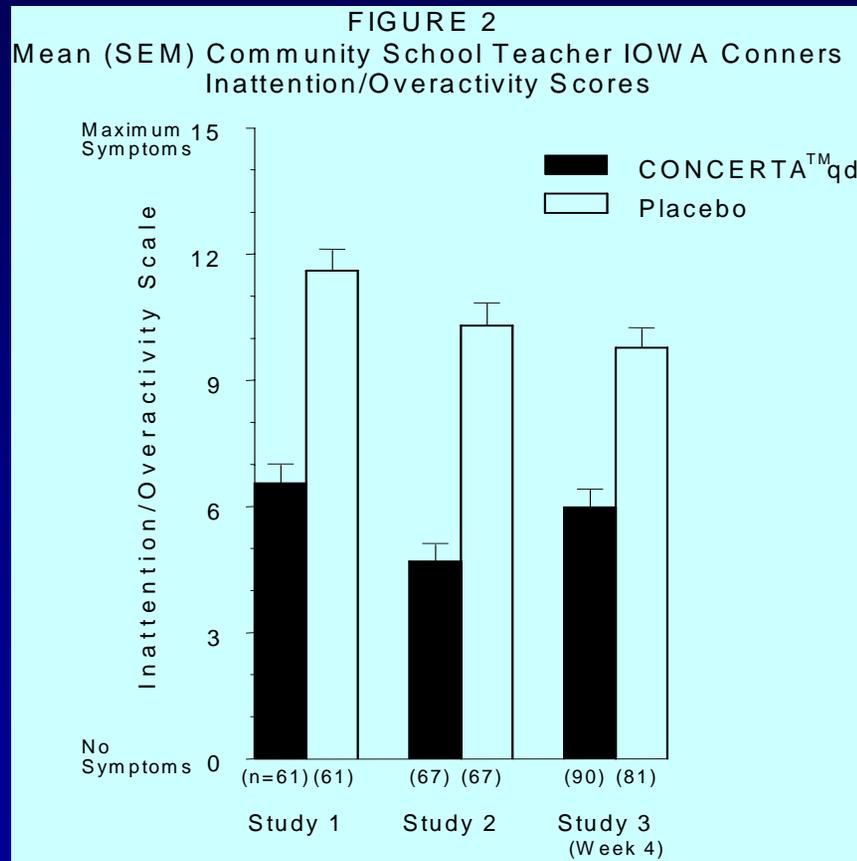
Drug Substance Changes

- Stereo-specific
 - 21-278 Focalin (dexmethylphenidate HCL) Tablets 11/13/2001
 - 21-802 Focalin XR
(dexmethylphenidate HCL)
Extended Release Capsules
5/26/ 2005

Basis for Approval

- Established Diagnosis of ADHD
- Improvement on Class Room Measures of Attention and Behavior in Double Blinded Randomized Placebo Controlled Trials
- *Swanson, Kotkin, Agler, M-Fynn and Pelham (SKAMP) laboratory school rating scale
- Inattention/Overactivity with Aggression (IOWA) Conners scale.

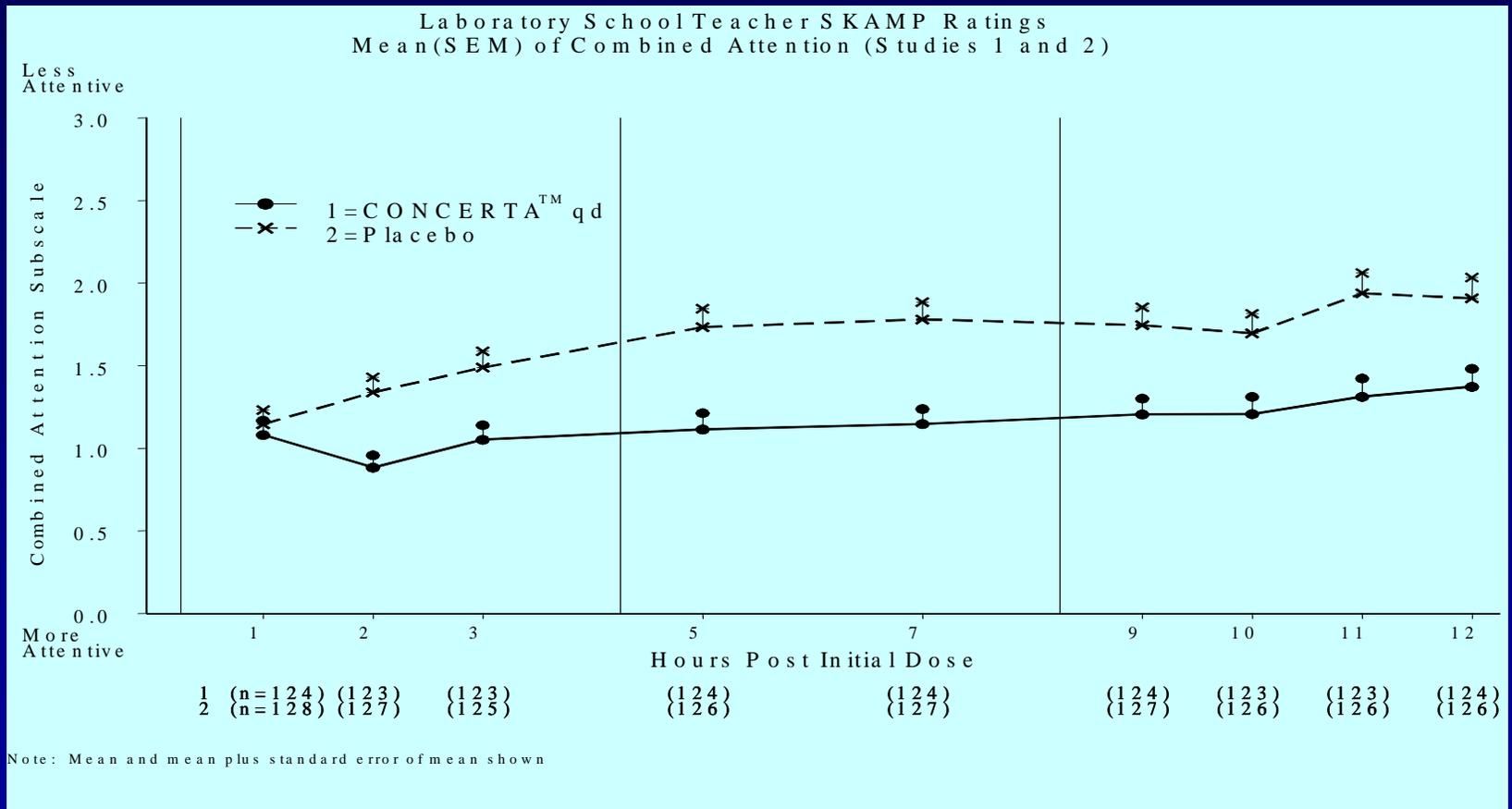
Studies Uniformly Positive



SKAMP SCORES

- **Attention Index**
 - **Getting started**
 - **Sticking to task**
 - **Attending to an activity**
 - **Making activity transitions**
 - **Completing assigned tasks**
 - **Performing work accurately**
 - **Being neat and careful while writing and drawing**
- **Deportment index**
 - Interacting with other children
 - Interacting with adults
 - Remaining quiet
 - Staying seated
 - Complying with teachers directions
 - Following classroom rules

Duration of Action Claim Tested throughout the day



Conclusion

- Stimulants are a very reliable mainstay in the treatment of ADHD
- Duration of action claims are based on significant success at multiple critical time-points
- Clinical benefit must always be weighed against adverse events
- Given the now broader background of the prescribing population-adverse events associated with stimulant treatment need to be labeled as accurately as possible