FDAAA: Landmark Shift In FDA Authority; Industry Practices

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A New Landmark

Kefauver “Efficacy” Amendments, August 1962

- Substantial evidence standard
- Advent of well-controlled clinical trial as the key to FDA approval


- Post-marketing risk management
- Advent of the well-identified patient population

Thalidomide Prevention Act

Thalidomide Control Act
Introductory message to FDA staff (May 2009)

- Praised FDA as the protector of public safety
  - The agency that kept thalidomide off the market in 1962
- Should have said:
  - FDA is the agency that figured out a way to keep thalidomide on the market for 11 years

FDA Commissioner Margaret Hamburg
Janus Effect

New NDA/BLA priorities

- Better designed NDAs/BLAs
- Redefines objective of clinical trials: find and identify responders and patient populations
- FDA will look for post-market control plans early in the development cycle

Giving FDA authority in post-market

- Mandatory Label Changes
- Look-back safety reviews
- Post-market surveillance
  FDA sees its new mandate as the “detection of safety problems…and rapid response”
New Approval Model

Not “YES” or “NO”

Few Patients, Tight Control; Premium Price

PM

Safe Access

Enhanced Communications

Labeling & Assessment

Mandatory Phase IV Trials

28 of 41 drugs approved in first 18 months of REMS era

More Patients, Less Control

How and To Whom

Entereg, Fentora, Onsolis

Tysabri, Thalomid, NPlate

Xenazine, Remoxy, Embeda, Botox

Cimzia, Banzel, Vimpat

Not "YES" or "NO"

More Patients, Less Control

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A Tiered Approval System

Control is "necessary to ensure that the benefits of the drug outweigh the risks."

(1) "known serious risk; (2) "signals of serious risk”; (3) “identify an unexpected serious risk.”

Patient-specific-monitoring, lab tests, registries

Specialties, limited pharmacies, hospitals only

MedGuides, Follow-up messages for docs, DTC rules

Timelines for re-review; Safety labeling authority

Mandatory Trials

Labeling & Assessment

Enhanced Communications

Safe Access

Few Patients, Tight Control

More Patients, Less Control
How Big Are The Changes?

FDA

✓ The Search for Responders:
   Even if a drug has only a 10% effect, “it might have a rather large effect in a fraction of the population.” There are plenty of opportunities in early studies to identify the responders and incorporate that information into the design of later-phase trials.
   -- FDA CDER Deputy Director Robert Temple

✓ FDA’s Role In Health Delivery
   FDA plans to be "a much more active player as part of the health care delivery system." The agency will be involved in "assuring that drugs are not only safe and effective if they’re used as labeled, but that they are safe and effective in real use and in the real world…”
   -- CDER Director of Executive Programs Deborah Henderson

Industry

✓ A New REMS Process
   BIO is already asking FDA for a schedule of REMS topics and meetings during IND/NDA phases: e.g. discuss patient inclusion and exclusion in relation to REMS at time of IND submission.
   -- Comments on FDA REMS Guidance

✓ Free Speech Challenge
   Allergan is challenging the authority of FDA to require warnings about off-label uses of Botox. FDA’s warnings “do not give physicians using Botox for spasticity specific guidance about how to further minimize that risk.”
   -- Allergan comments on October 1, 2009 suit filed in DC federal court
1. **FDA and health economics data**
   
   One of six mandatory post-market studies for *Prevnar-13* calls for Pfizer to conduct an “ecologic study to assess national trends in health care visits for otitis media in children younger than five years of age.” FDA requiring sponsors to collect general data about the impact of their products on health care system.

2. **Follow-on Biologics**

   Class REMS for botulinum products requires the three sponsors of the different brandname products to describe each product as different and difficult to switch -- substitutable-with-caution.

3. **Counter-detailing**

   Long a process of interest and debate on Capitol Hill – a way to get a more balanced message about new products/old products to the marketplace: REMS help address that objective.

4. **Comparative Effectiveness**

   Not happening now but FDA could require sponsors to inform the medical community about new comparative trial results. The new information would change the safety and risk/benefit profiles for existing products.
The Many Uses of REMS

- Marketing License
- Liability Shield
- Negotiating Leverage
- Savior of Drug Development?
Marketing License

Speaker’s Bureaus
Scripted Medical Science Liaisons
Aggressive Sales Force Goals
Prescriber Data Tracking
Targeted Journal Ads
“Seeding Studies”
Anti-Substitution Campaigns
Direct-to-Consumer Marketing
Marketing License?

**Targets of Industry Critics**
- Speaker’s Bureaus
- Scripted Medical Science Liaisons
- Aggressive Sales Force Goals
- Prescriber Data Tracking
- Targeted Journal Ads
- “Seeding Studies”
- Anti-Substitution Campaigns
- Direct-to-Consumer Marketing

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Marketing License

Speaker’s Bureaus

Scripted Medical Science Liaisons

Aggressive Sales Force Goals

Prescriber Data Tracking

Targeted Journal Ads

“Seeding Studies”

Anti-Substitution Campaigns

Direct-to-Consumer Marketing

Targets of Industry Critics

Mandated By FDA REMS
“Sanofi-Aventis will issue REMS Print Advertisements in the following professional society journals, monthly for 24 months, following approval of the REMS:

Journal of the ACC
Circulation
Annals of Internal Medicine”
FDA Orders A Speakers Bureau

Stepping Into Marketing Management

Xenazine (tetrabenazine): 40-year-old tranquilizer, approved by FDA last August for Huntington’s Disease –

- Prolonged and difficult three-year FDA review
- Suicidality concerns

- REMS for product includes “several educational vehicles”
  - “A trained Speaker’s Bureau which will include local and regional thought leaders”
  - Speaker materials must be cleared through FDA-DDMAC
FDA Centric View

Who Controls The Drug?

New Law Gives FDA The Upper Hand

Future Swings Will Never Return to Pre-2007 Center Point

The Pendulum Swing

…But What About The Big Picture?
Providers Push Back

“REMS with elements to assure safe use essentially create a whole new class of drugs from the delivery system and cost perspectives.”

“ASCO has noted with growing concern the process by which REMS are imposed without input from the physician community.”
Opioid REMS Will Be Largest Undertaking To Date
- Wake Up Call For Health Care System

76 Speakers During 2009 Meeting
- Patients, Providers, Pharma Too

"FDA considers the industry wide group as one of many stakeholders there to provide them with a view or some input, and then they will collate all this, interpret it, integrate it and then come up with a set of recommendations which we will then be mandated to implement.

"We have not been able to really sit down with the agency and discuss the best way forward for this novel and unprecedented activity. It has a laudable goal but we have got to get it right."

--One Pharma Exec
PDUFA V Comes Up In 2012
Questions?

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