

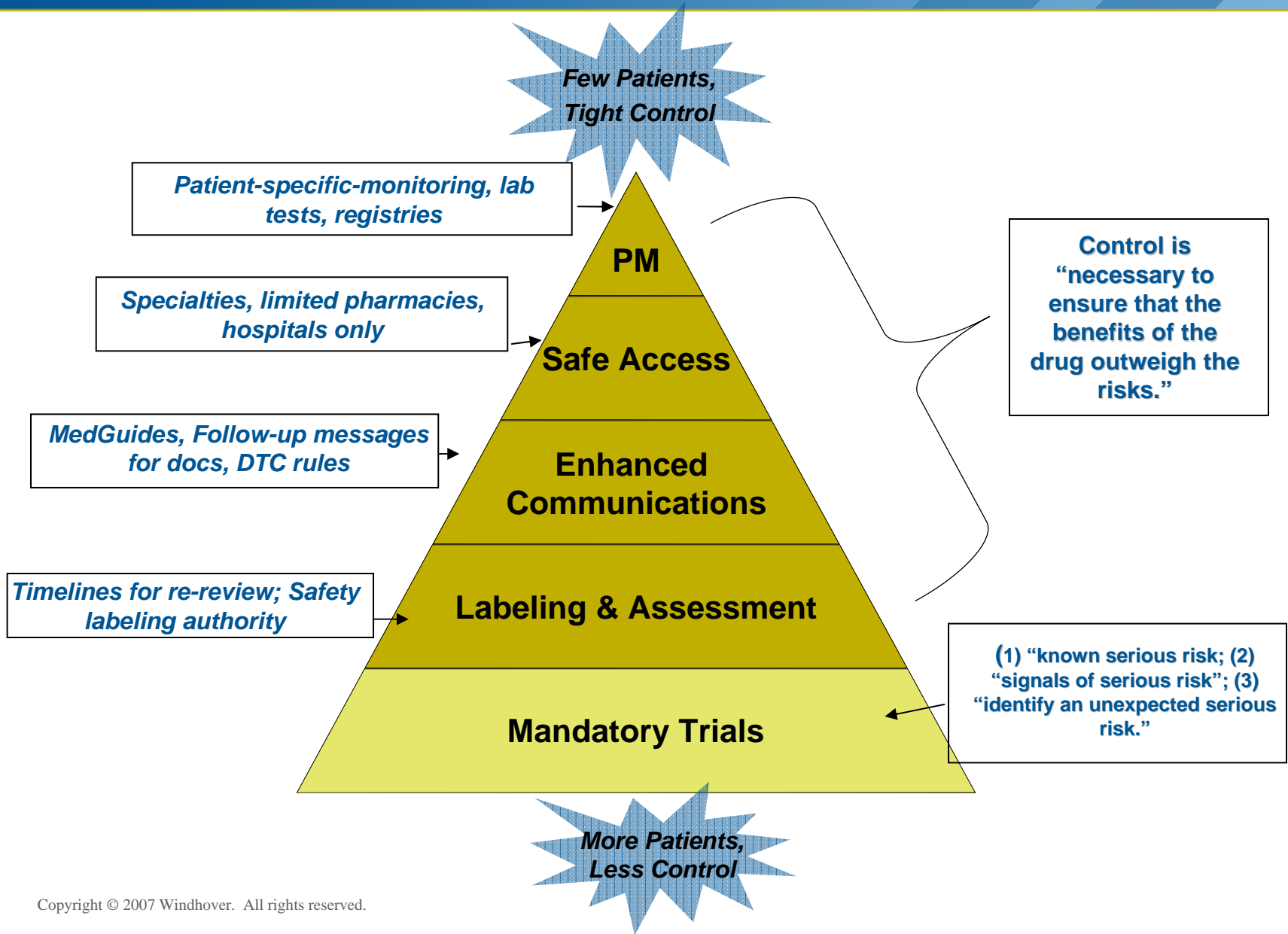
# FDA Rising

**Of all the interested parties in off-label (Justice, Congress, Courts, OIG), FDA has been surprisingly quiet in recent years. The agency appears ready to burst back on the scene.**

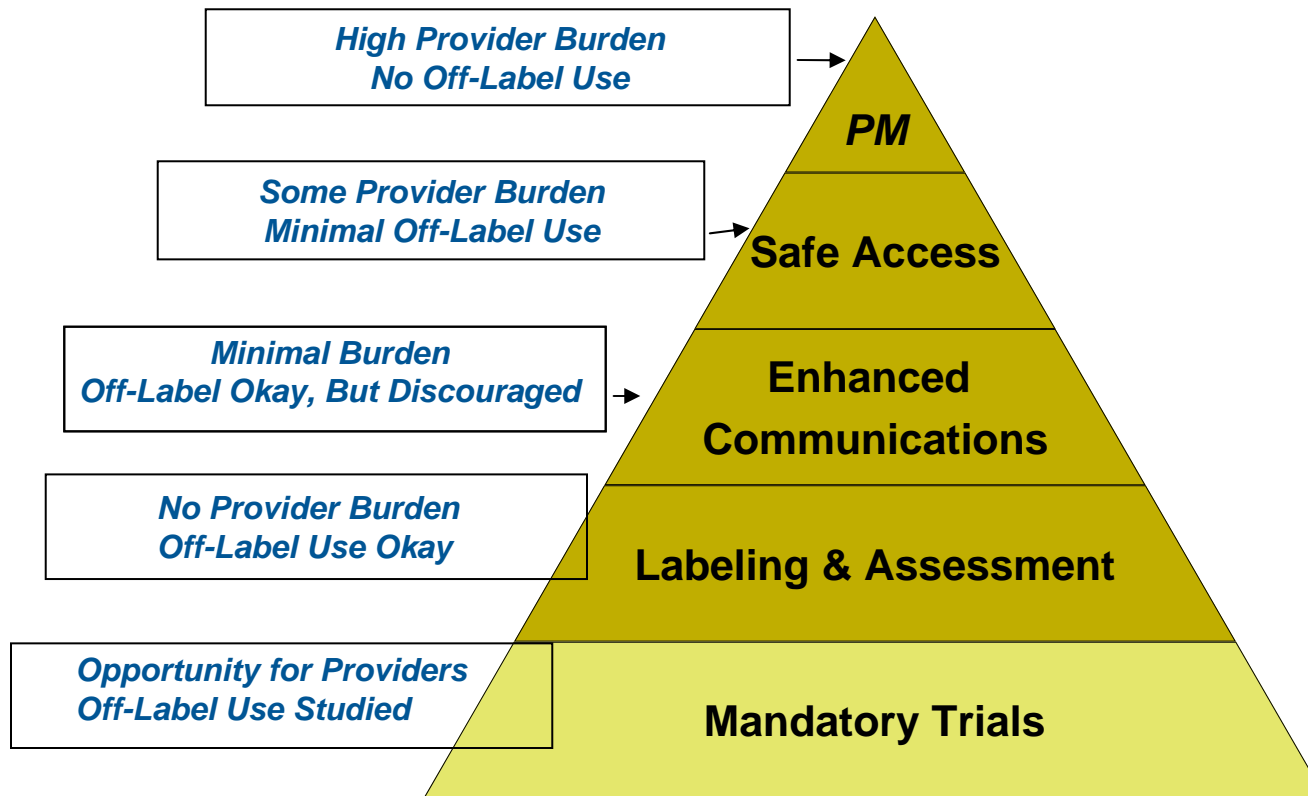


- **FDA started the furor over off-label in early 1990's**  
Kessler v. oncology community
- **Relatively quiet since WLF loss in late 1990's**  
Safe harbor approach – expired Sept. 2007  
Ceded enforcement to Justice Department, state attorneys general, and Office of Inspector General
- **New guidance from FDA**  
Sought by industry: create more clarity--while the climate remains more balanced
- **REMS authority from FDA Amendments Act**  
Risk Evaluation & Mitigation Strategies give agency a push into further postmarket controls

# FDAAA Tiers of Regulation



# REMS and Off-Label Use



- **Cephalon sought new indication for oral fentanyl: non-cancer breakthrough pain**
  - High level of off-label use (80%-plus) supported the sponsor's sense of a need for a new, approved indication
  - Sponsor offered to limit detailing for new indication – restricting to current physician users
- **Regulatory focus on postmarketing control**
  - Not traditional judgments on safety and efficacy from clinical trials; review focused on risk management plans and ability to control drug to defined populations
  - Sponsor's previous experience with risk management plans became key part of discussion: committees were not impressed
- **Preview of look-back authority**

- **Eventually, sponsors should expect questions on marketing/advertising plans as well as distribution controls during NDA process**
  - Part of the process of patient identification
  - FDA can justify the concern as a way to assure that marketing will not undercut other REMS efforts
- **Commitments made during NDA discussions raise an additional threat of off-label challenges**