Regulatory Issues Related to the Study, Approval and Promotion of Abuse Liability Indications and Abuse Resistance Claims

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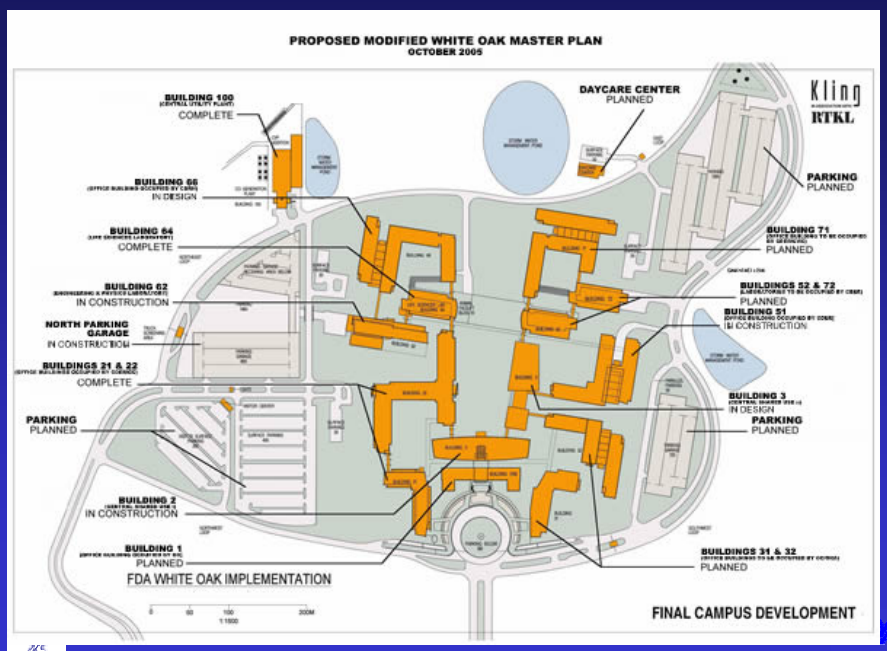
Office of New Drugs Update

- DACCADP and DAAODP have merged
- The new division is the Division of Anesthesia, Analgesia and Rheumatology Products (DAARP)
- Note the loss of the word “drug”
- We’ve also moved:


PROPOSED MODIFIED WHITE OAK MASTER PLAN
OCTOBER 2005
BUILDING 100
COMPLETE
DAYCARE CENTER
PLANNED
Kling
RTKL
PARKING
PLANNED
BUILDING 66
IN DESIGN
BUILDING 64
COMPLETE
BUILDING 71
PLANNED
BUILDING 62
IN CONSTRUCTION
BUILDINGS 32 & 72
PLANNED
NORTH PARKING GARAGE
IN CONSTRUCTION
BUILDING 51
IN CONSTRUCTION
BUILDINGS 21 & 22
COMPLETE
BUILDING 3
IN DESIGN
PARKING
PLANNED
PARKING
PLANNED
BUILDING 2
IN CONSTRUCTION
BUILDING 1
PLANNED
BUILDINGS 31 & 32
PLANNED
FDA WHITE OAK IMPLEMENTATION
FINAL CAMPUS DEVELOPMENT

Indications and Claims

- **Indications**
  - The approved uses and populations for a drug or biologic product
  - Off-label use is generally not regulated by the Agency
- **Claims**
  - May be based on any labeled information
  - As long as the claim is accurate and complete
  - May be explicit or implicit
  - Closely regulated by the Agency

Product Development Phase

- Appropriate studies should address:
  - The intended indication and population
  - The risk:benefit balance
  - Potential public health concerns, e.g. abuse liability; pediatric exposure
- FDA works closely with sponsors during this phase:
  - pre-IND, EOP2a, EOP2, Guidance, pre-NDA meetings
  - Comments on protocols; SPAs; Fast Track
  - Input from SEALD team
  - Dispute Resolution; Regulatory Briefings

Review Phase

- Frequent interactions between sponsor and review division
- 74-day letter
- Discipline letters, including comments from DDMAC, ODS, CSS, etc.
- Inspections
- Amendments
- Labeling negotiations
- Benefits of a first-cycle approval
- Advisory Committees

Post-Marketing

- Phase 4 commitments
- Adverse event reporting requirements
  - Review division
  - ODS
- Monitoring by DDMAC and Compliance
- Surveillance for special concerns, e.g. abuse, misuse and diversion
- Safety signals:
  - Patient and Prescriber Sheets
  - Health Advisory Alerts
  - Safety Monitoring Board
- RiskMaPs

Abuse Liability Indication: Why is the Bar So High?

- OxyContin (1995) label specifically stated that it would be less abused due to the extended-release formulation
- Clearly, this was not the case
- In fact, there was (and is) no data to support this claim
- This claim is thought to be one of the causes of the wide-spread abuse of the product
- Any future claims/indications will need to be based on data from adequate and well-controlled studies

Developing an Abuse Resistant Product

- Consideration of the patient population
  - Cannot decrease effectiveness
  - Cannot increase adverse events
- Consideration of the abuse population
  - Extent of abuse
  - How is the product abused?
  - How will abuse of the product affect the abusers?

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Studying Abuse Liability as an Indication

- The endpoints to be studied are:
  - reduced diversion and abuse in the community, and
  - a clear reduction in the complications associated with abuse
- Our best guess on study design: large epidemiological studies, carried out over an extended period of time
- The unknowns:
  - Feasibility?
  - Metrics?
  - Validity?

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Abuse Resistance Claims

- Implicit
- Explicit would require validation that the abuse resistance results in a reduction in abuse liability (thus, allowing for an actual indication)
- Can be any product feature that allows for a compelling likelihood that it will reduce abuse, e.g.
  - Incorporation of components that will cause unpleasant effects when an PO product is administered by non-PO routes
  - Physical barriers to crushing, melting or extraction
  - Addition of antagonists

Studying Abuse Resistance Claims

- Require careful evaluation of study methodologies, metric choices and analysis plans during development
- Require input and discussion from all appropriate Agency review staff during development
- Extent of the implicit claim is ultimately a matter for the review phase

Labeling and Promotion

- Labeling dependent upon adequacy of the data
- Results would be included in the appropriate section of the label, e.g., physical barriers in the product description section
- Promotion would be limited to presentations of the pertinent data without comment on or allusion to reduced abuse liability

Working Together to Reduce Abuse of Opioid Analgesics

- The Agency strongly encourages the development of abuse resistant opioid products
- The Division will work closely with sponsors to develop studies that will provide data to support claims in labeling
- The Division and DDMAC will work closely with sponsors to write labeling that provides a clear description of abuse resistant properties
- Promotion of abuse resistance, while necessarily implicit, will no doubt provide a marketing advantage