Expanded Access Programs
An Industry Perspective

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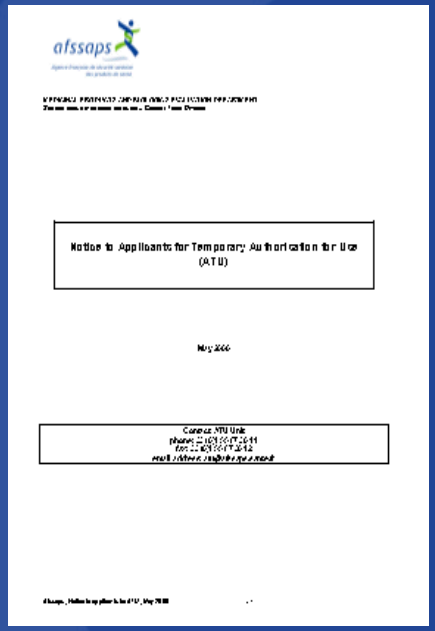
Expanded Access and Expedited Approval of New Therapies Related to HIV/AIDS

- **"Expanded access mechanisms are designed to make promising products available as early in the drug evaluation process as possible to patients without therapeutic options, either because they have exhausted or are intolerant of approved therapies."**
  - ~6% of salvage patients are unable to construct a suppressive regimen with currently available therapy
  - HIV Treatment Guidelines recommend starting ≥2 active ARVs in patients failing current therapy
  - EAPs are for a single new drug

http://www.fda.gov/oashi/aids/expanded.html

Expanded Access Programs
Multiple guidelines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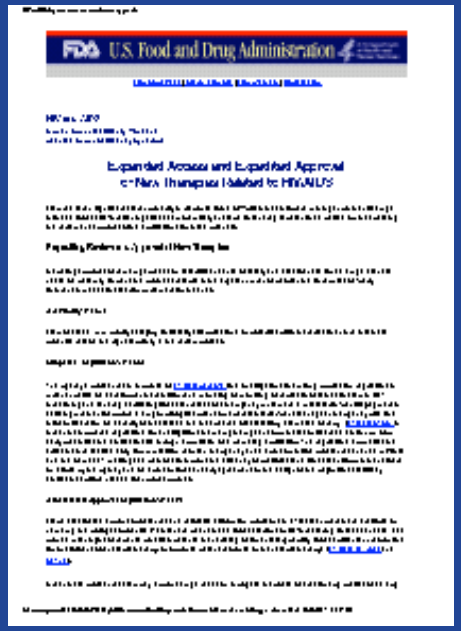
Notice to Applicants for Temporary Authorization for Use (ATU)

May 2006


U.S. Food and Drug Administration

Expanded Access and Expanded Approval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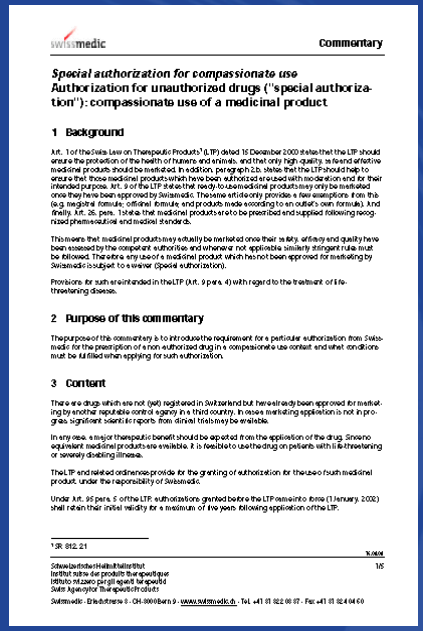
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Commentary

Special authorization for compassionate use

Authorization for unauthorized drugs ("special authorization"): compassionate use of a medicinal product

1 Background

2 Purpose of this commentary

3 Content

Multiple programs

- Expanded Access program/protocol (treatment IND)
- Open Label Safety Study
- Country Specific Programs (French ATU)
- Individual treatment IND – differ by country

Comparison of Phase 2b/3 Studies and EAPs

	Phase 2b/3 Studies	EAPs
Patients	Highly selected	More representative of overall population
Protocol	Complex and Highly controlled	More representative of real world care
Comparator	Gold standard therapy	None
Data collection	Extensive	Safety focused
Physicians	Experienced researchers	More representative of clinical care
Site payments	All study expenses paid	Frequently no payment
Site research staff	Highly trained	Frequently not available
Publications	High visibility	Also ran

Balancing Conflicting Priorities
Access to life saving medications

- **Patients want universal access for**
  - Hepatic impaired patients
  - Renal impaired patients
  - Pregnant women
  - Acutely ill patients
  - Patients with substance abuse or psychiatric issues
  - EAPs to pick up cost of routine care

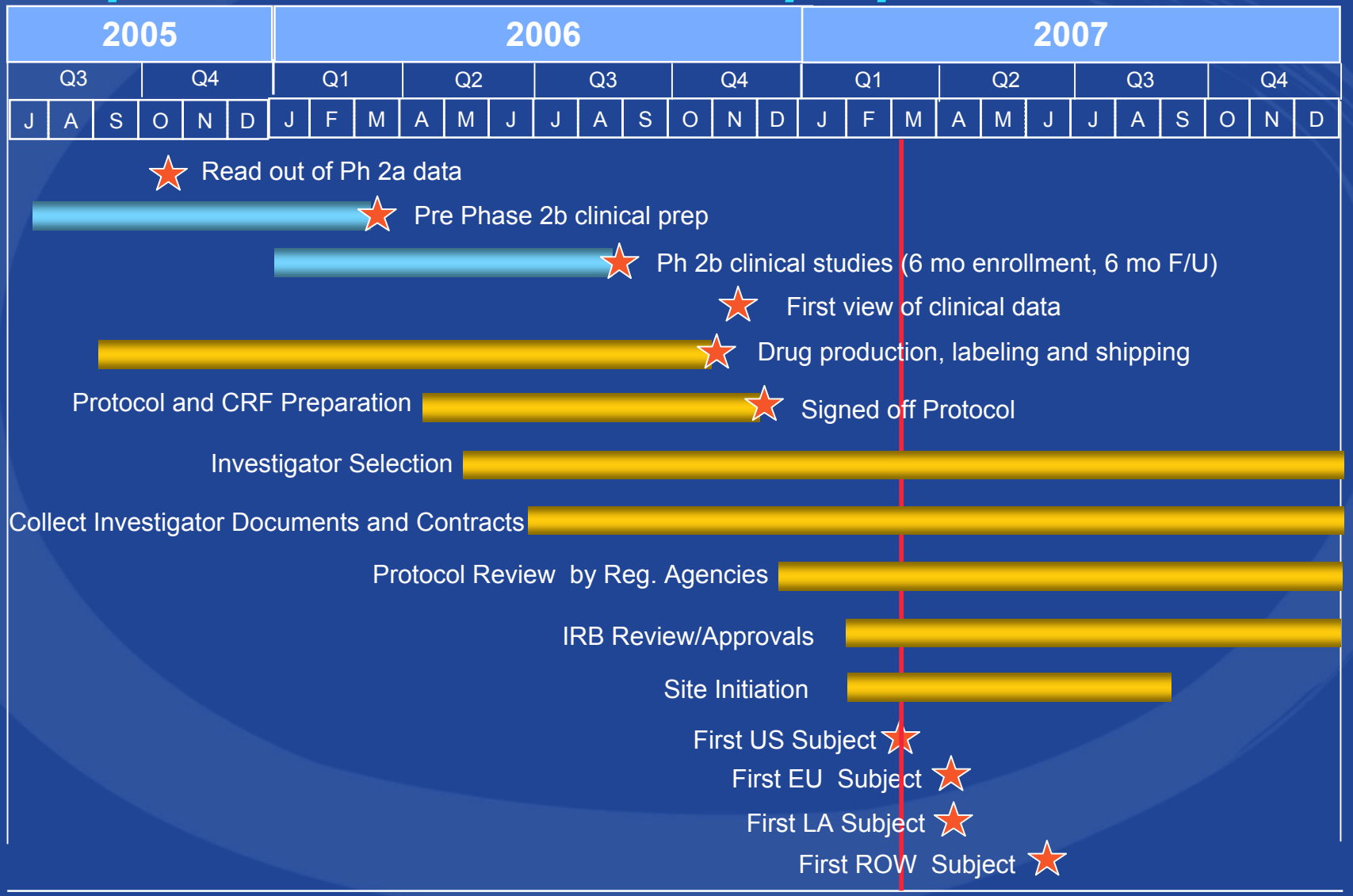
- **Physicians want fewer barriers to participation**
  - Easy access to new ARVs
  - Programs that last at least 6 months/ideally >1yr
  - Minimal paper work (data collection, drug management documentation)
  - Limited monitoring,
  - More interesting data collection
  - Not to lose money by participating in the EAP
  - More scientific publications

Balancing Conflicting Priorities
However drug is still experimental

- **Some regulators want more data before enrolling**
  - Hepatic impaired patients
  - Renal impaired patients
  - Pregnant women
  - Acutely ill patients
- **"Regulations" mandate**
  - Collection of all AEs
  - Monitoring similar to other clinical trials
  - Submission of every SAE to IRB/ECs
- **Companies want**
  - Single global EAP protocols
  - Safety profile reflective of the drug
  - Adequate data to determine causality for AEs
  - Opportunity to "train" treating community about appropriate use of the new therapy
  - Publications

Expanded Access Program

Require extensive "at risk" preparation



Making an EAP Successful

Plan for success, invest at risk

- **Open dialogue about EAP with advocates and physician advisors before you have Ph 2b clinical data**
- **Assure adequate drug for EAP**
  - Accurately project need/demand for drug 2.5 years before you have Ph 2b clinical data
- **Recruit physician investigators before you have clinical data**
- **Negotiate contracts before you have a final protocol**
- **Draft EAP protocol prior to having clinical data, finalize within 3 days of data read out**
- **Obtain simultaneous IRB/EC and regulatory review**
- **Staff up to execute EAP before Ph 2b clinical data are available**
- **Negotiate co-enrollment with other protocols for new ARVs (where permitted)**
- **Start drug-drug interaction studies with other experimental agents prior to either company knowing they have a drug**

Discussion

Expanded Access Programs offer interesting challenges but offer companies an opportunity to train treaters about new therapies while addressing unmet medical need while collecting a more robust safety database