

How to Navigate the FDA Regulatory Maze to Drug Approval in the U.S.

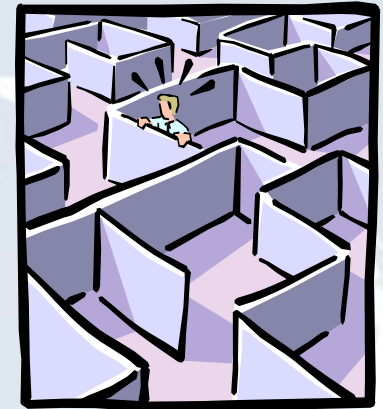
Harriette Nadler, PhD
VP Regulatory Affairs
DJA Global Pharmaceuticals Inc.

April 27, 2010



What are the different regulatory pathways?

505 (b)(1): Submitted for an innovator's product not previously approved; 'traditional' pathway; FDA user fees apply



505 (b)(2): *Generally* submitted for a change to a previously approved (usually innovative) product (Reference Listed Drug or RLD); relies on FDA's previous findings of efficacy and safety; cross references to innovator product literature permitted; FDA user fees apply even though process is simplified; 'streamlined' pathway

505 (j): Submitted for generics or duplicates (same administration route, dosage form, or strength) of approved products (i.e., RLDs); relies on FDA's previous findings of efficacy and safety. No user fees apply and no FDA meetings allowed. Specific advice re: pharmacokinetic study protocol permitted.

505 (b)(1), 505 (b)(2), and 505 (j) Pathways

Why does FDA use these numbers and letters?

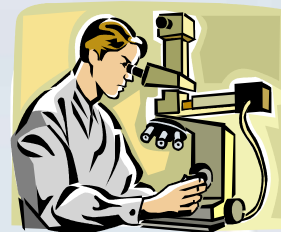
- Short hand designations for sections of regulations in Food Drug & Cosmetic Act that describe requirements for different routes for approval of new drugs

What are RLDs?

- **RLDs** are the most comparable products in terms of active ingredient, dosage form, route of administration, and strength to proposed product
- Applicable to 505 (b)(2) NDAs and ANDAs



Examples of requirements for 505 (b)(2) product approval in different scenarios



New injectable formulation in 2005: Abraxane®

(albumin-bound microfine particle suspension of
‘solvent-free’ paclitaxel, particle size in nano range (~100 nm)

RLD: Indication: ‘solvent-based’ paclitaxel

New Clinical Data:

- Single pivotal study in >220 patients with breast cancer compared **Abraxane®** vs RLD; pharmacokinetics required
- BA/BE studies not relevant for injectable

New Nonclinical (Tox) Data

*****LABELING- SECTION 14***:**

*Clinical data from single pivotal study of **Abraxane®** vs RLD*

- *Statistically significantly higher lesion response rate of **Abraxane®** vs RLD*