



NIPTE Center of Excellence for Abuse Deterrent Opioid Technologies: Assessment of current and future research needs in generic drug regulation of ADF formulations

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Research Needs

- Internal FDA studies
- NIPTE – Multi-institution Studies with Proven Expertise

APPROVED PRODUCTS WITH ADF LABELS

EXAMPLES of INTERNAL FDA STUDIES NEED

- Category 1
- Category 2
- Category 3
- Category 4



How was sameness determined after post marketing SUPAC related changes?

DPQR Lab Research



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Effects of excipients and curing process on the abuse deterrent properties of directly compressed tablets

Ziyaur Rahman^{a, b}, Ahmed S. Zidan^a, Maxwell Korang-Yeboah^a, Yang Yang^a, Akhtar Siddiqui^a, Daa Shakleya^a, Mansoor A. Khan^{a, b}, Celia Cruz^a, Muhammad Ashraf^a
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<http://doi.org/10.1016/j.ijpharm.2016.12.015>

Assessing impact of formulation and process variables on in-vitro performance of directly compressed abuse deterrent formulations

Ziyaur Rahman^a, Yang Yang^a, Maxwell Korang-Yeboah^a, Akhtar Siddiqui^a, Xiaoming Xu^a, Muhammad Ashraf^a, Mansoor A. Khan^{a, b}
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<http://doi.org/10.1016/j.ijpharm.2016.02.029>

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Risk based *in vitro* performance assessment of extended release abuse deterrent formulations

Xiaoming Xu^a, Abhay Gupta^a, Manar Al-Ghabeish^a, Silvia N. Calderon^b, Mansoor A. Khan^{a, c}
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<http://doi.org/10.1016/j.ijpharm.2016.01.031>

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External Studies Needed

- Understand the CMA and CPV that affect the CQA of **ALL PRODUCTS** with HEAD-ON RLD Comparisons!
- Develop tests and evaluation methods for nasal irritation and other studies of importance to FDA
- Link the CQAs with attributes of category 2 and category 3 markers
- Bring NIPTE Center for ADF Expertise to bear (Purdue, Texas A&M, Maryland, UT Austin and others have expertise and infrastructure – All needed research can be completed within three years

Will provide generic product approval pathway with three scenarios

Scenario 1

| Composition of Oxycodone HCl ER Tablet (80mg) | | | |
|---|-------------|---------|---------|
| RLD | | | |
| Sponsor | | PR1 | PR2 |
| ANDA Number | | | |
| DMF Holder | | | |
| Strength (mg) | | | |
| Core Tablet | | % (w/w) | % (w/w) |
| | Function | | |
| Oxycodone HCL USP | Active | x1 | x1 |
| PEO, NF | CR Poly | x2 | - |
| | Filler | | x2 |
| Lactose | | | |
| Hypromellose USP | CR Poly | | x3 |
| Povidone | Binder | | x4 |
| BHT | Antioxidant | | - |
| IPA | Gran.Aid | | - |
| Colloidal SiO2 | Glidant | | x5 |
| Mg.Stearate NF | Lubricant | x3 | x6 |

Very different designs and composition

No ADF Test results Submitted – High risk

Negative Control C may have a role in ADF test development

Review - Major deficiencies..

Scenario 2

- Composition (of highest 80 mg strength)

| Ingredient | Function | RLD | Generic |
|---------------|----------|-----------|-----------|
| Oxycodone HCL | | 80 mg | 80 mg |
| Exc 1 | | x1 mg | x1 mg |
| Exc 2 | | x2 | x2 |
| Exc 3 | | x3 | x3 |
| Exc 4 | | x4 | x4 |
| Exc 5 | | x5 | x5 |
| Total | | t1 | t2 |

Exactly the same grades and quantity of excipients - identical composition

- Manufacturing process

| Unit Operations | RLD | Generic |
|-----------------|-----|---------|
| Unit op1 | Yes | Yes |
| Unit op2 | Yes | Yes |
| Unit op3 | yes | No |
| Unit op4 | Yes | Yes |

Minimal ADF tests submitted

Review - Risks involved – deficiencies..

Scenario 3 -

- Composition (of highest 80 mg strength)

| Ingredient | Function | RLD | Generics |
|---------------|----------|-----------|-----------|
| Oxycodone HCL | | 80 mg | 80 mg |
| Exc 1 | | x1 mg | x1 mg |
| Exc 2 | | x2 | x2 |
| Exc 3 | | x3 | X3 |
| Exc 4 | | x4 | x4 |
| Exc 5 | | x5 | x5 |
| Total | | t1 | t2 |

Exactly the same grades and quantity of excipients - identical composition

- Manufacturing process

| Unit Operations | RLD | Generics |
|-----------------|-----|----------|
| Unit op1 | Yes | Yes |
| Unit op2 | Yes | Yes |
| Unit op3 | yes | Yes |
| Unit op4 | Yes | Yes |

All ADF tests done with direct head-on comparison

No risks involved – Approvable by Cat 1 studies
Why negative control here?

Exact same manufacturing process