Excipients and processes: Ensuring successful development and scale-up of solid particles for extended release

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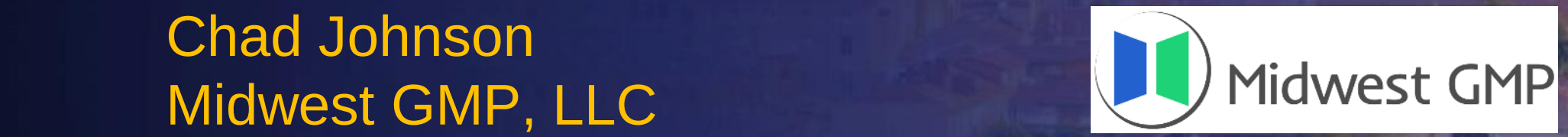

CONTROLLED RELEASE SOCIETY
CRS 2024 Annual Meeting AND Exposition
JULY 8-12, 2024 • BOLOGNA, ITALY
INTEGRATING
Delivery Science
ACROSS DISCIPLINES

My Background

- Education in chemical engineering and biomedical engineering

- New to the controlled release pharmaceutical field

- Almost 20 years in the medical device field
    - Many roles
    - Concepts are similar

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Midwest GMP

- cGMP manufacturing
- For early clinical trials
- Documentation
- Scale-up
- Storage

Why build out Midwest GMP?

- Project was ready for initial human phase I clinical trial

- Attempted to outsource cGMP manufacture – either too expensive or very long timelines due to insufficient capabilities/expertise

- Decided to build out capabilities both for internal and external projects
  - Goal to fill this underserved need to bridge the ‘valley of death’

Are you ready for human testing?

- Advancing a technology too soon can result in a multitude of problems
- Need to have a good grasp on both critical quality attributes and critical process parameters

Is the design truly frozen?

- Can be hard to stop trying to improve design
- What ifs can hurt project
- Chasing shiny objects

Details Matter (including the small ones!)

- During scale-up to cGMP manufacture little details can become big issues
- Understanding sources of uncertainty can help planning

Critical Process Parameters (CPP)

- Chemicals (sourcing, storage, controls)
- Formulation (how, when, vessels)
- Time (at least, no more than, range)
- Temperature (how to control, measure)
- Physical forces (mixing, pumping)
- Product movement
- Storage conditions before, after, during

There are other concerns

- Waste management
  - Movement, storage, disposal
- Hazardous chemicals
  - Handling, personnel protection
- Water
- Daily run times

Sticker shock - cGMP is expensive

- Facilities and trained personnel
- Specialized equipment
- Cleaning and sterilization
- Disposables where possible
- Verifications and validations
- Documentation
- Testing

…And it takes longer than you think it should

During scale-up, problems will occur

…I have always found that plans are useless but planning is indispensable
- Eisenhower

- No matter how much you prepare, there will be issues
- Exploratory runs find some problems – but not all
- Focus on crucial steps – understand what has big impacts
- Build in flexibility whenever possible, or at least understand the impact

Perfect is the enemy of good

- Bridging the ‘valley of death’ where promising research never gets out of the lab
- Clinical trials are only way to move the field forwards
- All the questions cannot be answered prior
- Seek help when necessary

Dans ses écrits, un sage Italien
Dit que le mieux est l'ennemi du bien
- Voltaire

Better a diamond with a flaw than a pebble without one
- Chinese proverb

Perfection is the enemy of progress
- Churchill

Thank you!

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