BEST PRACTICES FOR MODELING – FINITE ELEMENT ANALYSIS FOR COMBINATION PRODUCT DESIGN VERIFICATION

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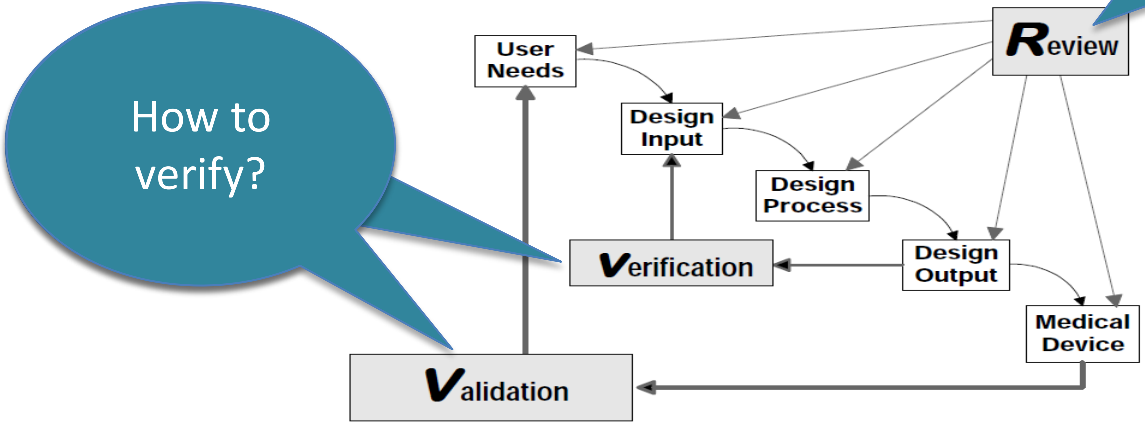
UBM

Waterfall design process

As a packaging or device system design engineer,



Verify the system design using 1st principles and modeling works, and perform the testing to confirm the theoretical analysis!!

Contents

1. Introduction – benefits from 1st principles and modeling
2. Prefilled syringe combination products – manual and auto injector
3. A syringe based auto injector system design verification
   a. Case study 1: Semi-finished syringe design verification focusing on plunger and barrel
   b. Case study 2: Syringe based auto injector system design verification
4. Conclusions

Introduction – benefits from 1st principles and modeling

1. 1st principles and modeling (e.g., finite element analysis) can simulate situations that hard to prepare for testing.
2. Modeling can cover the entire design space (e.g., min & max), so it is a good example of QbD (Quality by Design) paradigm.
3. Robust and reliable system design can be achieved.
4. New parts, materials and designs can be quickly assessed.
5. Good root cause analysis tool for unexpected situations.

Note: Modeling verification is rigorously performed with experimental results.

Prefilled Syringe combination products

Manual prefilled syringe

Auto injector with the prefilled syringe operated by the spring force

Image source: BD website

Dynamic operation: spring force, plunger speed, coefficient of friction, air bubble volume, hydraulic pressure, etc.

Off-the-shelf syringe and auto injector, then why we need to perform design verification activities?

Design Verification plan

Individual system design verification

Semi-finished syringe with product

- Glide force
- Container closure integrity
- Others

Auto injector

- Tolerance stack-up
- Stress from drop
- Others

Total system design verification

Syringe based auto injector system

- Injection time
- Dose accuracy, etc.

Ultimate goal: Inject drug as designed

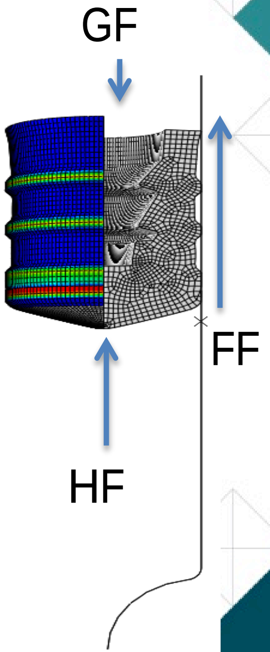
Case study 1. Semi-finished syringe design verification

➢ **Critical design factors: container closure integrity, glide force, etc.**

- Contact pressure from rubber plunger compression against the barrel
  - Hyperelastic and nearly incompressible rubber mechanical properties
  - Non-linear material models for stress-strain
- Glide force from frictional force and hydraulic force
  - Frictional force = COF x plunger contact force
  - Hydraulic force determined from Hagen-Poiseuille equation

$$\Delta P = \frac{8\mu L Q}{\pi r^4}$$

μ: product viscosity
L: needle length
Q: flow rate
r: needle radius



Note: Finite element analysis (FEA) modeling can estimate frictional forces and deformation of the rubber plunger.

Modeling DOE and FEA Results

- Sample: 1 mL long syringe (ISO standard)
  - Plunger OD: 6.8 to 7.0 ± 0.1 mm
  - Barrel ID: 6.35 ± 0.1 mm
- Parameters to determine the glide force and sealing pressure: plunger OD, barrel ID, needle ID & length, product viscosity, injection speed, rubber formulation, plunger design, etc.

e.g., Plunger OD (3) x Barrel ID (3) x Product Viscosity (3) = 27 combinations

Plunger OD (mm)	Barrel ID (mm)	Interference fit (mm)	Product viscosity (cP)	Estimated Glide force (N)	Estimated Sealing pressure (MPa)
6.7	6.25	0.225	0	1.5	1.6
6.9	6.25	0.325	0	2.5	2.2
6.9	6.35	0.275	1	2.6	1.9
6.7	6.45	0.125	6	4.0	1.0
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Robust and reliable system design verification covering the entire design space!!

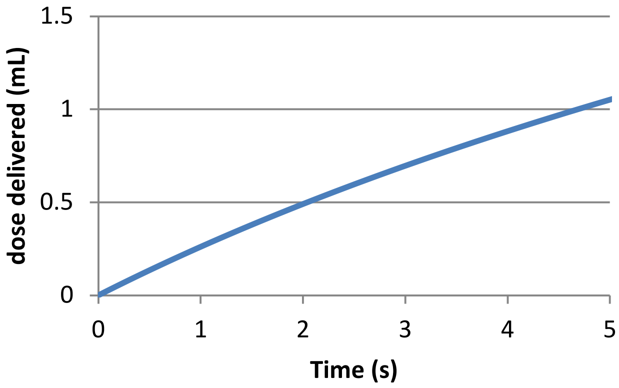
Case study 2. auto injector system design verification

- **Critical design factors: injection time, etc.**

- Dynamic operation: spring force, speed of plunger movement, air bubble volume, COF, and hydraulic force are dynamically changed.
- Plunger frictional study – develop a mathematical relationship between glide force, speed of plunger movement and hydraulic pressures e.g., glide force = A + B × Ln (speed) + C × hydraulic pressure.
- Develop differential equations and solve variables using a numerical solution tool. (e.g., Mathcad, Excel with Macro, FEA-CFD co simulation)

Modeling results – injection time

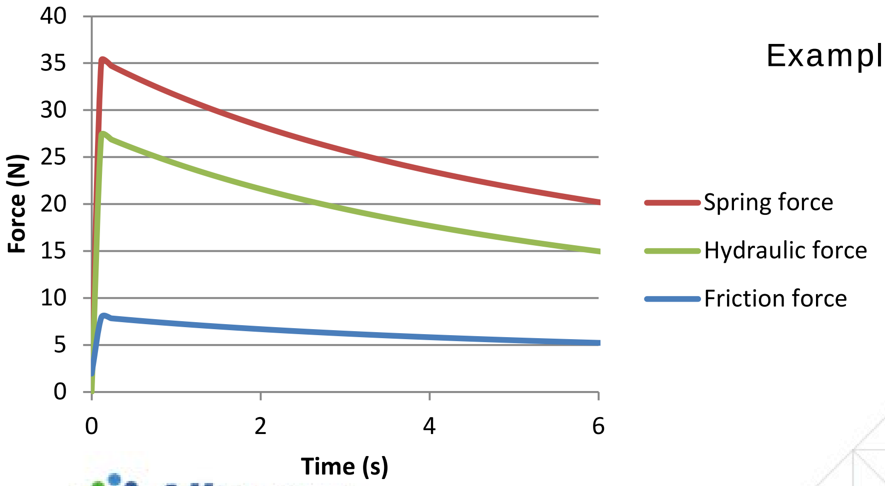
- The amount of drug delivered over time can be estimated.
- The dosing time can be estimated using different springs, product viscosity, fill volume, needle gage & length, etc.
- The model can be easily verified with experimentally determined dosing time.



Example: 15 cP solution
1 mL long syringe
27G TW needle.

Modeling results – force balance

- During the injection, the force is balanced.
  - Glide force (or spring force) = frictional force + hydraulic force
- Most of the spring force is used to dispense the liquid via a tiny diameter needle
- Better to work on needle to reduce the injection time instead of working on the plunger design, especially for a high viscosity drug.



Example: 15 cP solution
1 mL long syringe
27G TW needle.

Conclusions

1. Modeling is a powerful QbD tool to cover the entire design space.
2. First principles and modeling can minimize non-essential work but maximize necessary work.
3. Overall, the cycle time for a robust syringe and auto injector system design verification can be reduced.
4. Necessary process to design complex syringe and auto injector system from a proliferation of new drug formulations and injection mechanisms.
5. High confidence in selecting or designing new syringe and auto injector systems.

Conclusions (continued)

To enhance the design assurance level, let's put more efforts on 1st principles and modeling activities!!

Modeling &
1st principles

Experimental
results