Inspection of Ocular Drug Delivery Implants

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ABSTRACT

Ocular implants treat diseases such as glaucoma and macular degeneration with long-term drug release. The small size of the implants (diameter < 500 µm, length ~5 mm) presents challenges for handling, inspection, weighing, and measurement to ensure the quality of the implants.

At clinical stages, ocular implants are commonly 100% inspected for dimensions to ensure product fits into administration devices. Weighing 100% of parts to ensure proper API dose is also desirable but presents a major challenge: Implants weigh approximately 1 mg, requiring sensitive balances that are slow to stabilize and susceptible to static and other factors.

For material with a consistent density, part volume is a good surrogate for part mass. To demonstrate this, representative ocular implants were prepared by extrusion and cut to size. An automated inspection system (Keyence LM-1100) was programmed to recognize implant shape, then measure length, diameter, and cut angle of implants. The software calculated volume of the parts. Parts were weighed to evaluate whether volumetric specifications adequately captured mass specifications.

Analysis demonstrated the utility of using volume as a surrogate for mass for samples of consistent density. All units that passed volumetric specifications also met assay requirements (nominal target ± 10%). A strong correlation between measured volume and assay reinforced the utility of this approach for efficiently inspecting small implants.

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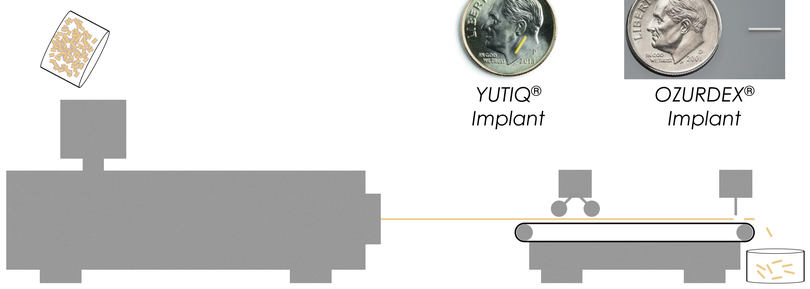
MANUFACTURING IMPLANTS

Sample Production

- Polymer/API mixture prepared by hot melt extrusion
- Twin screw extrude to diameter
- Cut to length in automated or manual system
- Batch size of 10,000 parts



YUTIQ® Implant

OZURDEX® Implant

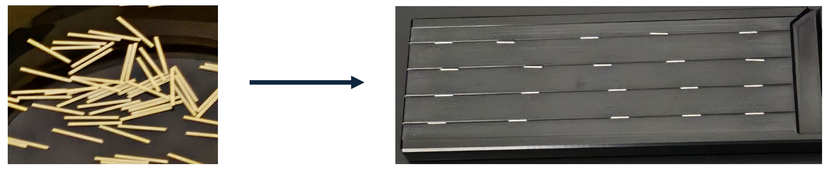
MANAGING SAMPLES

Challenges

- Ocular implants are <500 µm x <6 mm rods and weigh 1 mg
- Highly susceptible to static
- Difficult to control for inspection
- Time consuming to handle and organize

Solutions

- Ionized atmosphere, grounded equipment to reduce static
- Fixture to organize and track many parts simultaneously



MEASURING DIMENSIONS

Challenge

- Manual measurement of dimensions (e.g., by caliper) is tedious and slow

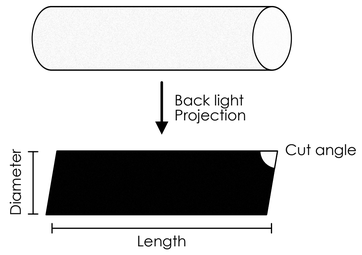
Solution

- Automate dimension measurements with Keyence LM-1100 inspection scope

1

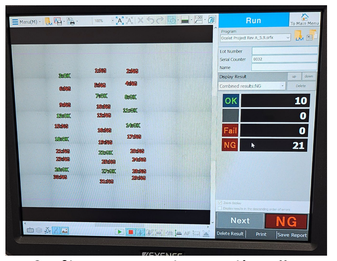
Sort parts for gross defects
Organize for measurement

2



Scope recognizes profile
Measures diameter, length, cut angles

3



Software automatically identifies parts that **PASS** or **FAIL** all specifications

SETTING IMPLANT SPECIFICATIONS

Challenge

- Implants must meet specifications for dosage and dimensions, driven by clinical needs
- Weighing 1 mg implants is exceedingly slow
- Dose (assay) measurement is destructive – cannot measure 100% of implants

Solution

- Define length and diameter requirements
- Establish density of implants
- Use density to set volume specification as surrogate for mass specification
- Dimension/Volume measurement is non-destructive – can measure 100% of implants

Product Needs

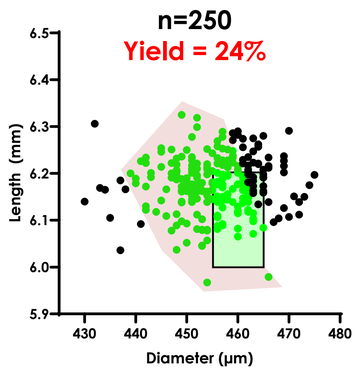
Fit in 21 Ga needle	Intravitreal administration	Treat ocular disease for 3 months
(Diameter)	(Diameter, Length)	(Drug load/Assay)

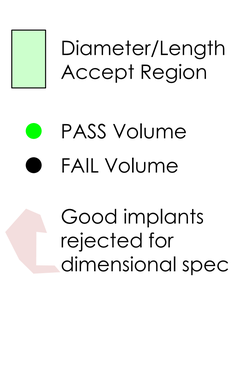
Diameter/Length Range Specification

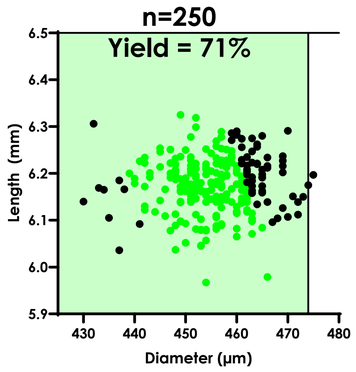
Diameter = 460 ± 0.05 µm ← Needle range
Length = 6.1 ± 0.1 mm ← Anatomy range
Assay = 95 – 105 % Label Claim ← Tx Duration

Volume Range Specification

Diameter < 474 µm ← Needle limit
Length < 6.5 mm ← Anatomy limit
Volume = 0.986 ± 0.049 mm^3 ← Drug load/Tx Duration







$$V_{implant} = \frac{m_{implant}}{\rho_{implant}}$$

Where:

$$m_{implant} = \frac{m_{API}}{w_{API}}$$

$$V_{implant} = \pi \left(\frac{d}{2}\right)^2 l$$

w_{API} = weight fraction API

Volume Range specification ensures highest yield of implants

CONCLUSIONS AND FUTURE CONSIDERATIONS

Our work shows that small ocular implants can be effectively managed, inspected, and measured through a combination of fixtures and semi-automated inspection scopes. Approaching ocular implant specifications from a volume perspective ensures maximum yield for clinical and commercial processes. Future work will explore the impact of surface area on elution properties of ocular implants.