Lonza Engine®
Accelerate Innovation

ABSTRACT AND ARTICLE
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WHITEPAPER: LONZA ENGINE® & XCELODOSE®

ACCELERATING PRE-CLINICAL AND CLINICAL TRIAL PATHWAYS WITH TARGET DOSING TECHNOLOGIES

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Abstract

Learn how Lonza helps developers quickly assess new drug candidates while minimizing API consumption through efficient excipient screenings, encapsulation and early-phase clinical development technologies.

Drug developers continue to face numerous pressures advancing active pharmaceutical ingredients (APIs) into commercial drug products. The push to reduce the time, personnel resources and capital expense involved in developing finished drug products is unrelenting.

Most of the time, candidate compound selection and synthesis process can be costly in its early stages. It can cause potential constrained API dosing evaluation and slow critical development paths relative to overall program timelines (which are becoming shorter).

To face these challenges, pharma's innovators are increasingly engaging the expertise of clinical development and manufacturing (CDM) partners to accelerate the process of putting drug products into human trials. One solution capable of accelerating speed-to-clinic timelines and reducing costs is to dose standalone API with no excipients into a capsule with microdosing technologies.

Answering the needs of drug developers, the Lonza Engine® equipment portfolio including the Xcelodose® technology, a powder microdosing system, helps developers quickly assess new drug candidates while minimizing API consumption. Our technical and formulation experts can provide further support on excipient screening, encapsulation and early-phase clinical development technologies.

(READ FULL ARTICLE)

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Full Article

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Drug developers continue to face numerous pressures advancing new drug candidates into commercial drug products. The push to reduce the time, personnel resources and capital expense involved in developing finished drug products is unrelenting.

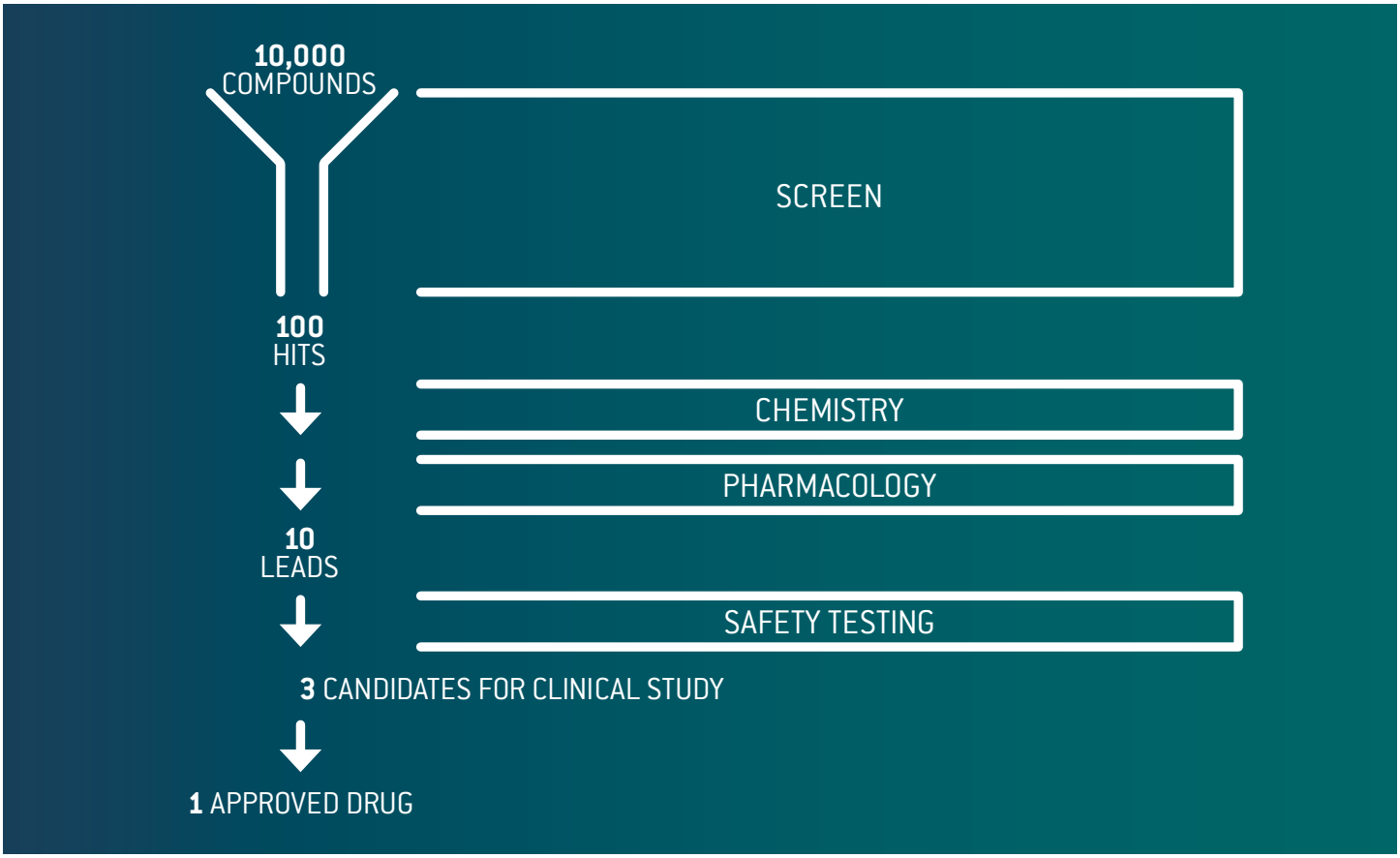
Most of the time, candidate compound selection and synthesis process can be costly in its early stages, causing potential constrained API dosing evaluation and slow critical development paths relative to overall program timelines (which are becoming shorter).

The main challenges for drug developers

According to FDA statistics, 60% of new drug launches in 2019 were designated in one or more expedited categories of fast track, breakthrough, priority review, and/or accelerated approval.[1]

These targeted regulatory pathways only add further to the time and financial pressures faced by small, and virtual pharmaceutical companies that develop the vast majority of early phase compounds today.

To meet expediated timeframes, drug developers are seeking solutions to help get the drug to consumers quickly as possible, while saving on development costs. This can mean pharmaceutical companies are managing a multitude of challenges through the early clinical trial stages.



Challenge #1
Managing multiple drug candidates

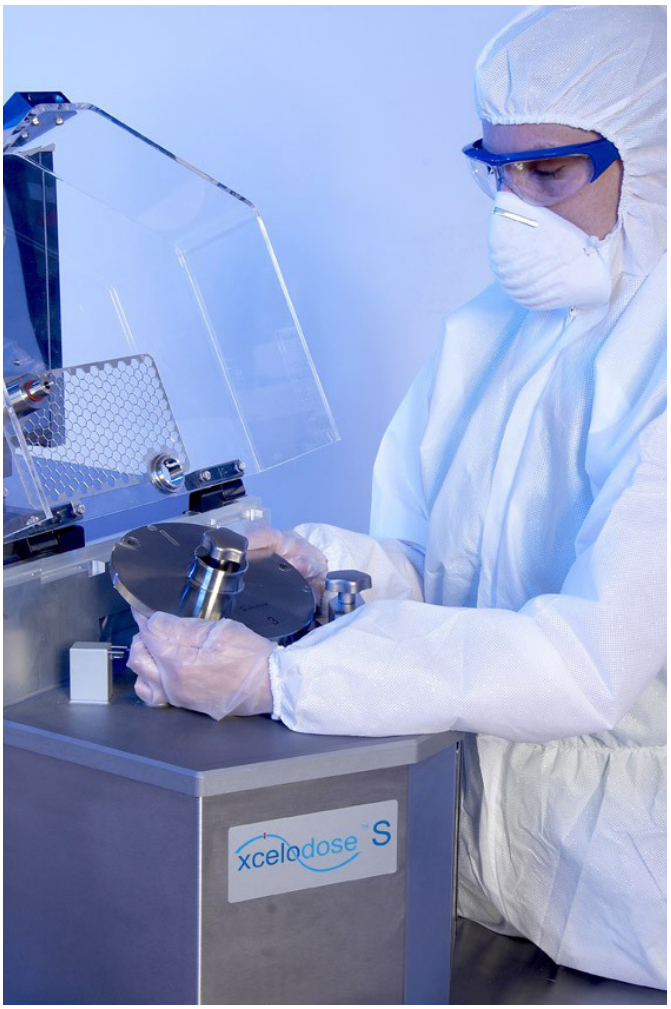
To help accelerate market timelines, drug manufacturers are often testing multiple drug candidates in early-stage clinical studies to ensure commercial success. Studies have shown that for every new drug brought to the market, estimates suggest that researchers will typically have tens of thousands of compounds to evaluate before development leads to a single[1] approved drug.[2]

During trials, researchers aim to use as little of the candidate formulation as possible to keep costs down, but also accurately test for efficacy.

Pharma innovators have employed microdosing technology to help accelerate speed-to-clinical trial timelines. Microdosing involves intricate handling of powdered formulations and the accurate dispensing of very small volumes into each capsule.

Challenge #2
Finding the correct excipient

Often times, excipients are added to the active pharmaceutical ingredient (API) to add volume or aid in flow properties during the capsule filling process. It is critical that excipients used are carefully evaluated to avoid interference with the active ingredients in the drug product formulations. Additionally, the mass and flowability of each excipient is important for an accurate distribution of the API in capsule without adding segregation issues. Blend and Content Uniformity testing is performed to maintain the strength during the encapsulation procedure. Compatibility excipient studies can take many weeks and can be expensive, adding hours and costs to each potential candidate.



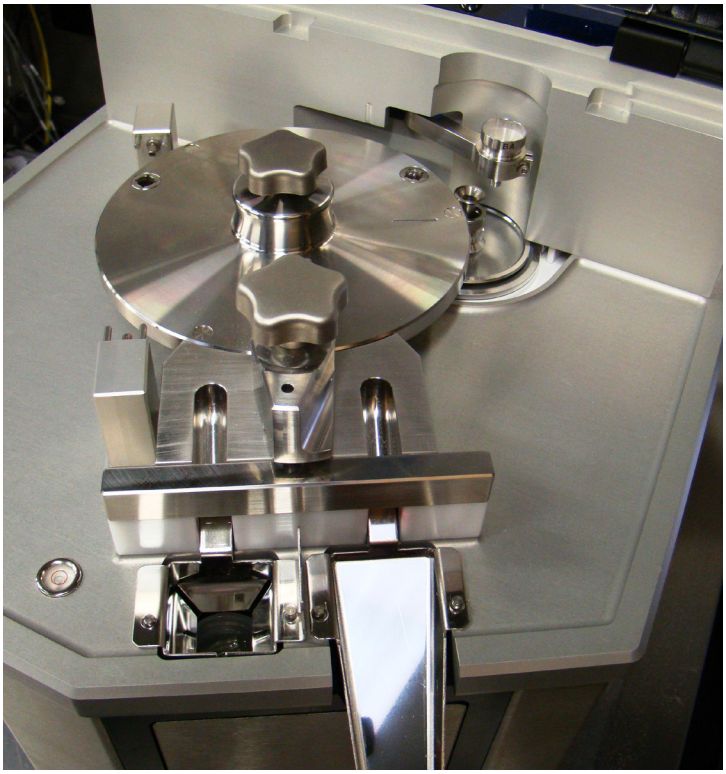
Challenge #3
Ensuring consistent amount of the active ingredient in each capsule

Once an ideal excipient is identified, it now needs to be mixed appropriately with the candidate API and filled in a capsule. It is vital during this step that the same amount of API is always fed in each single capsule. If the process is not done properly, due to the several physical parameters in play including flowability, electrostaticity, stickiness, density, and weight, it may result in a wrong dosage of API within the final capsule.

Drug developers need to consider the:

- Physical characteristics of APIs such as segregation, particle size, and morphology.
- Powder flow properties which can affect weight variation.
- Environmental effects on drug substance playing a factor in the flow and filling characteristics of the formulation.

A variation in the dosage could mislead the results of the clinical trials, by giving wrong feedbacks like stronger side effects or not properly treating the disease.



Lonza Xcelodose® powder microdosing system is the new solution

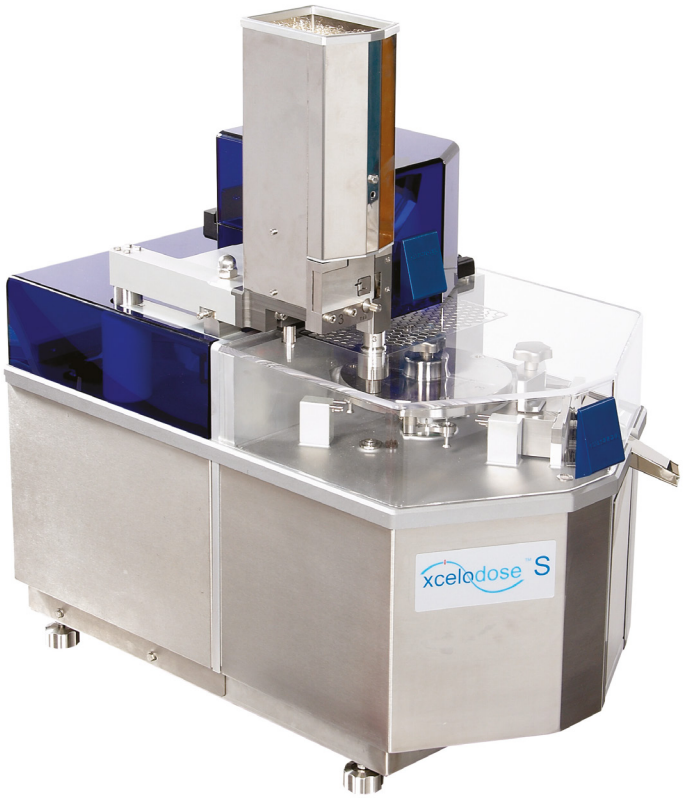
Answering the needs of drug developers, the Lonza Engine® equipment portfolio including Lonza Xcelodose® powder microdosing system has been created to help developers quickly assess new drug candidates while minimizing API consumption through efficient and accurate encapsulation.

The Lonza Xcelodose® system provides consistent dose accuracy by precise filling of capsules — without excipients or bulking agents.

How can the Lonza Xcelodose® powder microdosing equipment help with the process

Engineered for the precision weighing of drug substances, direct blends, or formulated blends in various capsule sizes ranging from Size 4 to 00 with typical weights ranging from 0.1 mg to 100 mg per capsule the Lonza Xcelodose® system offers scaled solutions that provide distinct economies for pre-commercial development including the ability to:

- Provide faster more precise filling and accurate drug substance dose dispensing.
- Minimize drug substance usage in formulation development.
- Deliver comprehensive compliance documentation with every weight dispensed through CFR21, Part 11 software.
- Delay excipient compatibility screening until after drug candidate selection is complete.
- Simplify analytical and stability evaluations.
- Focus analytical and formulation development spending.
- Migrate production to clinical supply using the same process.
- Deliver financially sustainable pathways to commercialization.



CASE STUDY:

FASTER TIME TO FIRST-IN-HUMAN

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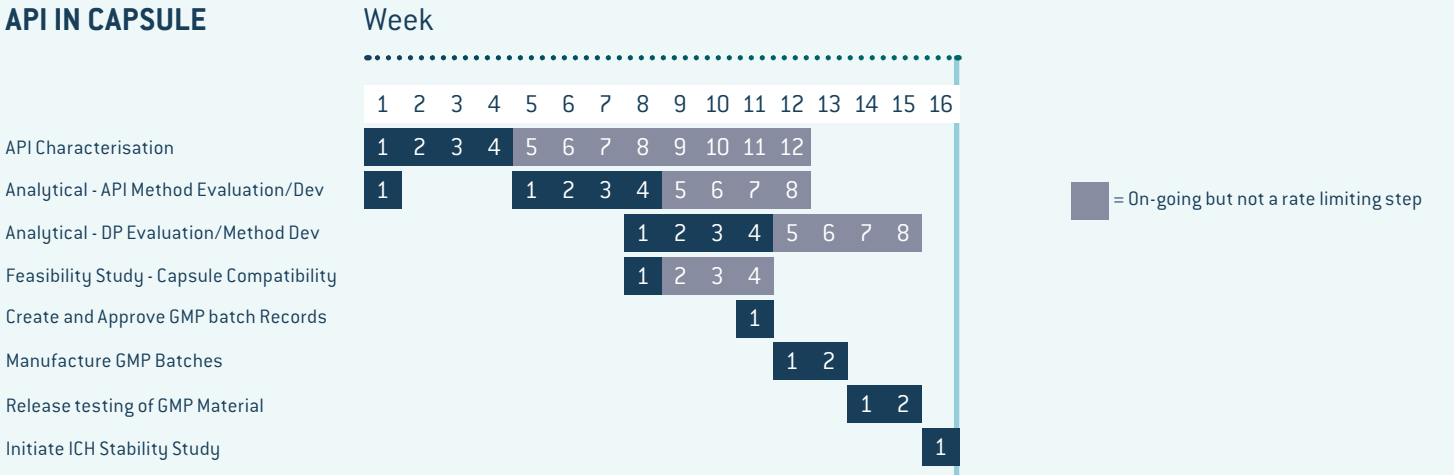
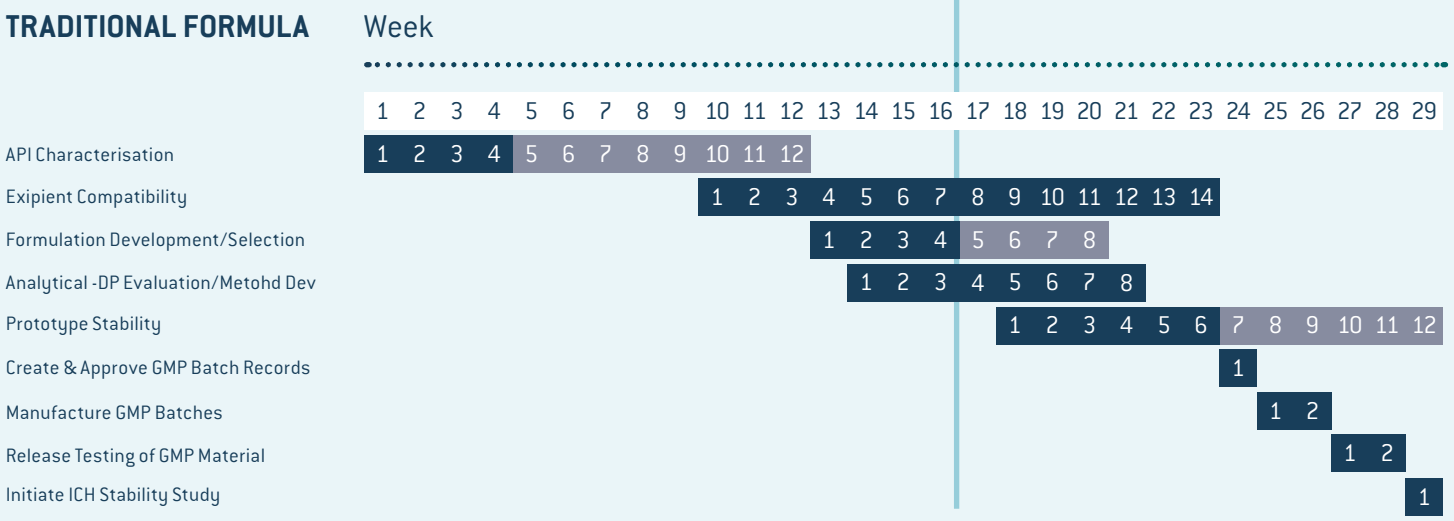
Microdosing programs using the Lonza Xcelodose® systems can be completed 45% faster than traditional formulation efforts, a reduction of 13-17 weeks from development time.[3]

In an internal study, Lonza compared the number of weeks taken from API characterization to first stability study using API-in-capsule against traditional formulation.
The result: Using an API-in-capsule cut development time nearly in half.





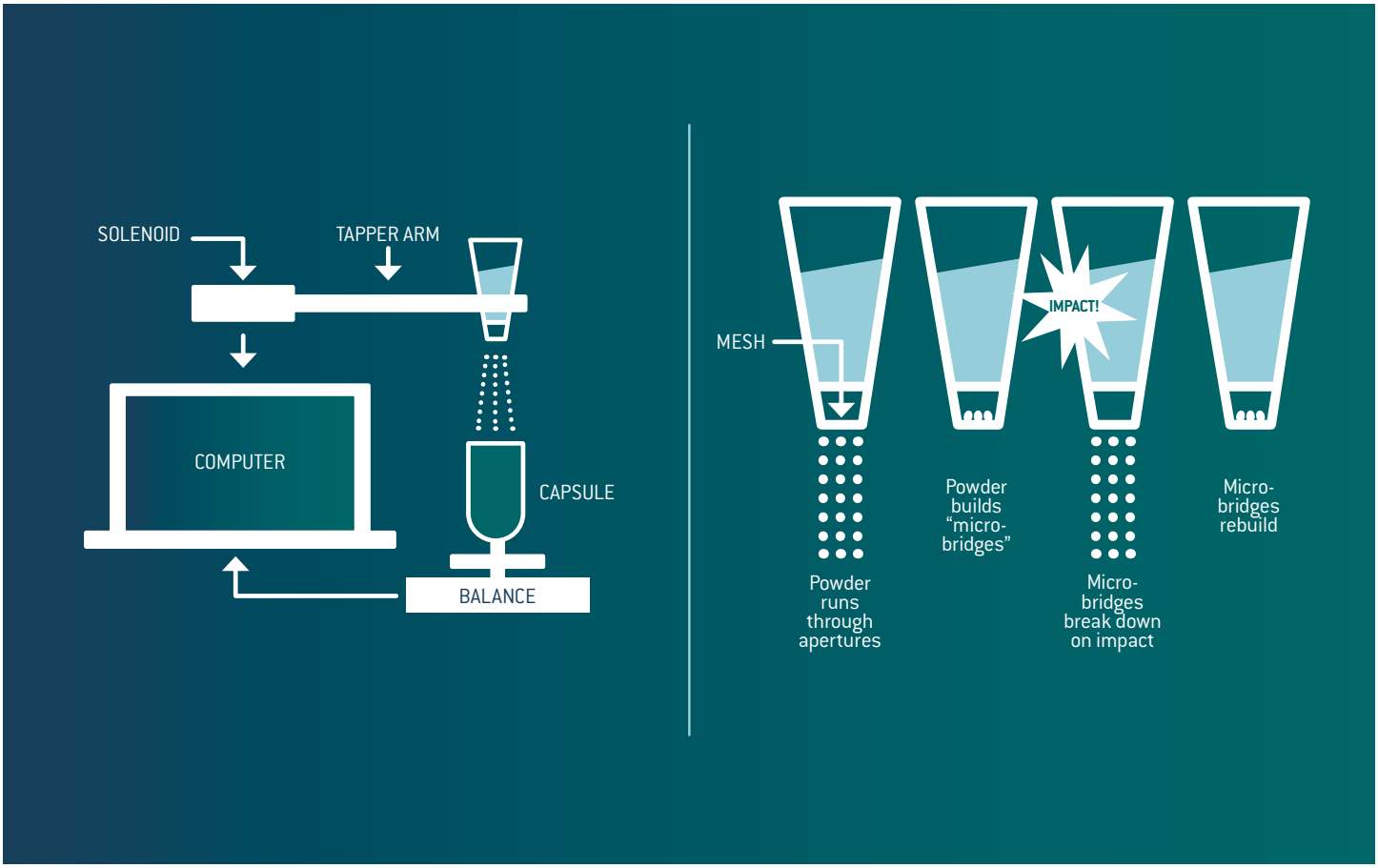
Source: *Dr Paul Skultety, Xcelience webinar 'Formulation Development Options for Speed to Phase I Studies', 2010*

Supported by highly precise and accurate automated systems, the benefits of the methodology can be far-reaching in terms of robust conclusions, data integrity and ultimately program success.

The Lonza Xcelodose® system excels at accelerating microdosing operations in the production

The system eliminates manual operations while automating others for increased accuracy, compliance, and operational efficiency:

- Controller estimates number of taps required to reach target weight
- Fill weight is monitored throughout the process
- The capsule is weighed while being filled (gravimetric feeding)
- Consistent weight is controlled through an algorithm adjusting to powder variability in real time
- Balance settles after last tap and then final fill weight is recorded
- Capsule labelled pass or fail according to user-defined tolerance bands
- Intuitive operator high visibility HMI (human machine interface) control system
- Summary reporting (pdf file) generated after each campaign



Summary

To serve pharma's developers better, Lonza offers an integrated portfolio of technologies designed to help quickly assess new drug candidates while minimizing API consumption through efficient excipient screenings, encapsulation and early-phase clinical development technologies.

The Lonza Xcelodose® microdosing system provides for consistent dosing and precise filling of capsules without added excipients.

- For pharma companies, this can mean a shorter drug development process facilitated by a reduction in formulation development.
- For any drug developer implementing automated solutions this can reduce labor costs and negate quality control issues associated with manual filling routines, while advancing in parallel analytical and prototype stability studies.

Ultimately this reduces the time taken to reach the 'first in man' clinical trial decision point, which allows to accelerate the throughput of candidate compound screening and speed up their development and their journey to patients.

[1]https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2019

[2]https://www.sciencedirect.com/topics/nursing-and-health-professions/drug-development

[3]Dr Paul Skultety, Xcelience webinar 'Formulation Development Options for Speed to Phase I Studies', 2010

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