Development of Potency Assays for Cellular Therapies

[in a Nutshell]

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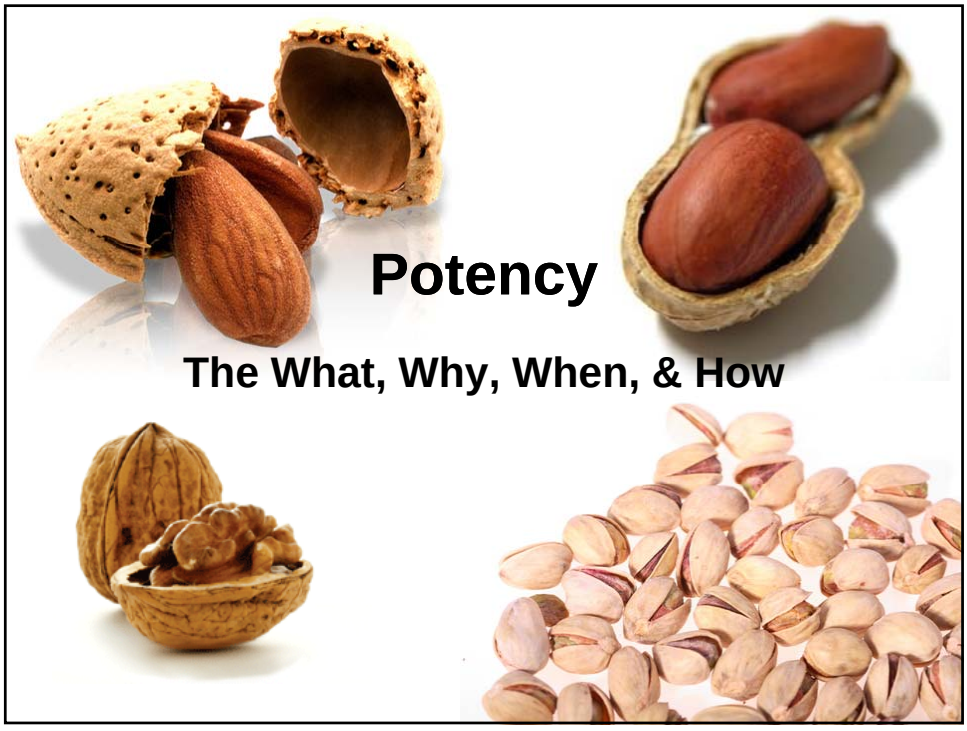

Potency

What?

…"the **specific ability or capacity of the product**, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, **to effect a given result**." [21 CFR 600.3(s)].

FDA/CBER Guidance for Industry: Potency Tests for Cellular and Gene Therapy Products (Draft Guidance), October 2008

Potency

What?

Regulations stipulate that "[t]ests for potency shall consist of **either in vitro or in vivo tests, or both**, which have been **specifically designed for each product** so as to indicate its potency in a manner adequate to satisfy the interpretation of potency given by definition in § 600.3(s) of this chapter." (21 CFR 610.10).

FDA/CBER Guidance for Industry: Potency Tests for Cellular and Gene Therapy Products (Draft Guidance), October 2008

Potency

Why?

[Beyond being obvious…]

All biological products **must meet prescribed requirements** of safety, purity and **potency** for BLA approval (42 U.S.C. 262, Federal Food, Drug and Cosmetic Act, (FDC Act) (21 U.S.C. 321 et seq.); 21 CFR 601.2).

FDA/CBER Guidance for Industry: Potency Tests for Cellular and Gene Therapy Products (Draft Guidance), October 2008

All potency assays used for release testing of licensed biological drug products must comply with applicable biologics and cGMP regulations including:

- Indicate potency (biological activity/activities) specific to the product (21 CFR 600.3(s) and 610.10; and 21 CFR 210.3(b)(16)(ii));
- Provide test results for release of the product (21 CFR 610.1; 21 CFR 211.165(a))
- Provide quantitative data (21 CFR 211.194; see also 21 CFR 600.3(kk); 21 CFR 211.165(d); 211.165(e););
- Meet pre-defined acceptance and/or rejection criteria (21 CFR 211.165(d); see also 21 CFR 600.3(kk); and 21 CFR 210.3(b)(20));
- Include appropriate reference materials, standards, and/or controls (see; 21 CFR 210.3(b)(16)(ii) and 211.160);
- Establish and document the accuracy, sensitivity, specificity and reproducibility of the test methods employed through validation (21 CFR 211.165(e) and 211.194(a)(2));
- Measure identity and strength (activity) of all active ingredients (21 CFR 211.165(a); see also 21 CFR 210.3(b)(7));
- Provide data to establish dating periods (see 21 CFR 600.3(l) and 610.53(a))
- Meet labeling requirements (21 CFR 610.61(g)(3) and 610.61(r))

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Potency
When?

Please be advised that you will be required to **establish** a potency assay **before initiating Phase 3 trials** and **validate** this assay **prior to submission of a license application**. Your potency assay should be a measure of "the specific ability or capacity of the product…to effect a given result".

Recent Summary of Pre-IND Call (FDA/CBER/OCTGT) for an MSC-based IND

Potency
When?

ASAP because…
There are a number of advantages, such as allowing you to:

- Demonstrate product activity, quality and consistency throughout product development
- Generate data to support specifications for lot release
- Provide a basis for assessing manufacturing changes
- Evaluate product stability
- Recognize technical problems or reasons a different assay might be preferable
- Evaluate multiple assays
- Collect sufficient data to support correlation studies, if necessary

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Potency

How?

- **Biological assay** – potency in a living biological system (in vivo animal, in vitro organ, tissue, cell culture)
- **Non-biological analytical assay** – surrogate of biological activity; immunochemical, biochemical, molecular attribute with correlation to biological activity
- **Multiple assays** (assay matrix) – should have at least one quantitative component

Using progressive implementation…

- Early product development
- Later phase product development
- Biological license
- *Much more detail in the Draft Guidance

FDA/CBER Guidance for Industry: Potency Tests for Cellular and Gene Therapy Products (Draft Guidance), October 2008

But what about early clinical phase investigations?

- FDA concurs that it **may not be possible to meet all of the requirements** expected for licensed biological products.
- **However, you still must submit data** to assure the identity, quality, purity and strength (21 CFR 312.23(a)(7)(i)) as well as stability (21 CFR 312.23(a)(7)(ii)) of products used **during all phases of clinical study**.

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But what about early clinical phase investigations?

- "[T]he **amount of information** needed to make that assurance **will vary with** the **phase** of the investigation, the **proposed duration** of the investigation, the **dosage form**, and the **amount of information otherwise available**." (21 CFR 312.23(a)(7)(i)).

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On to an example…

A potency assay for T regulatory cells…

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Thank you!

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