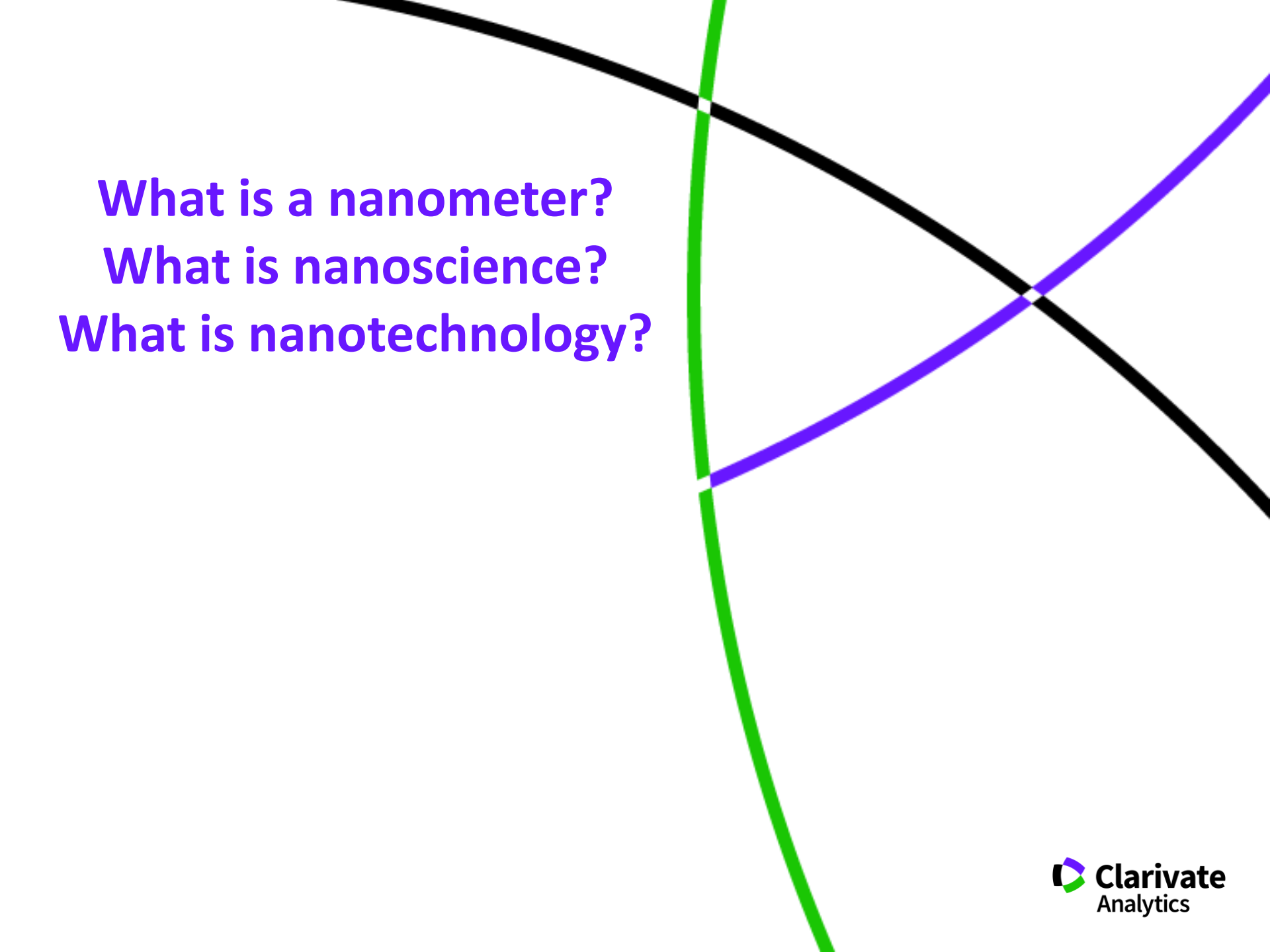


Nanotechnology Regulation: Regulatory guidance on using nanotechnology in medical devices

Anette Breindl, Senior Science Editor
BioWorld

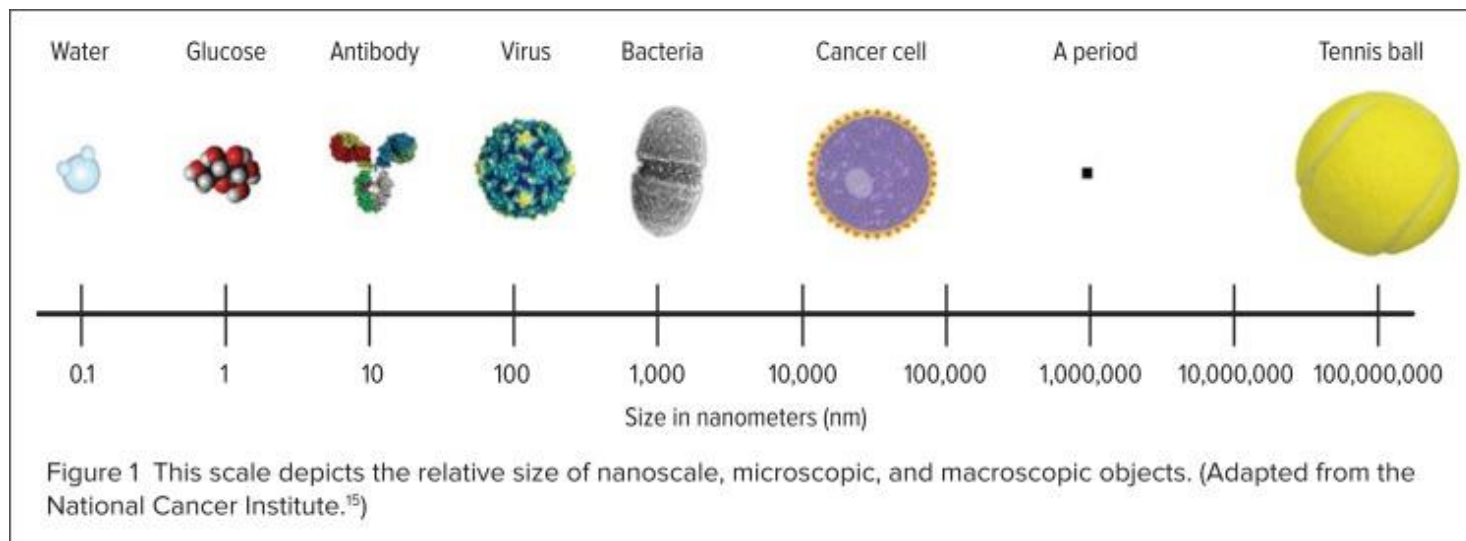
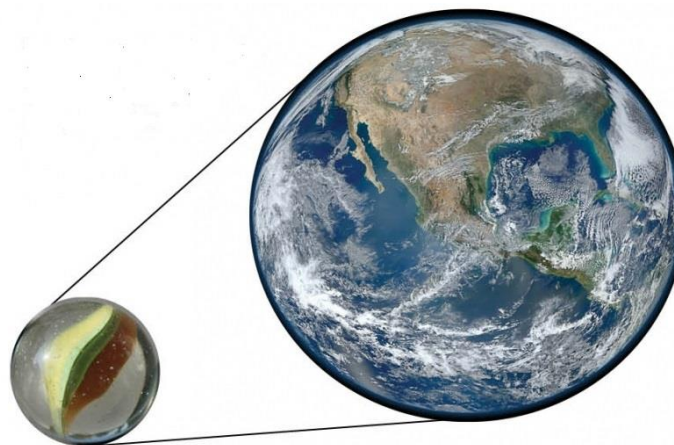
Mark McCarty, Regulatory Editor
BioWorld MedTech

October 2018



**What is a nanometer?
What is nanoscience?
What is nanotechnology?**

What is a nanometer?



What is nanoscience?

- “The study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale” Royal Society



Image credit: British Museum

What is nanotechnology?

- “The design, characterisation, production and application of structures, devices and systems by controlling shape and size at the nanometre scale” – Royal Society



Image credit: *Nature*

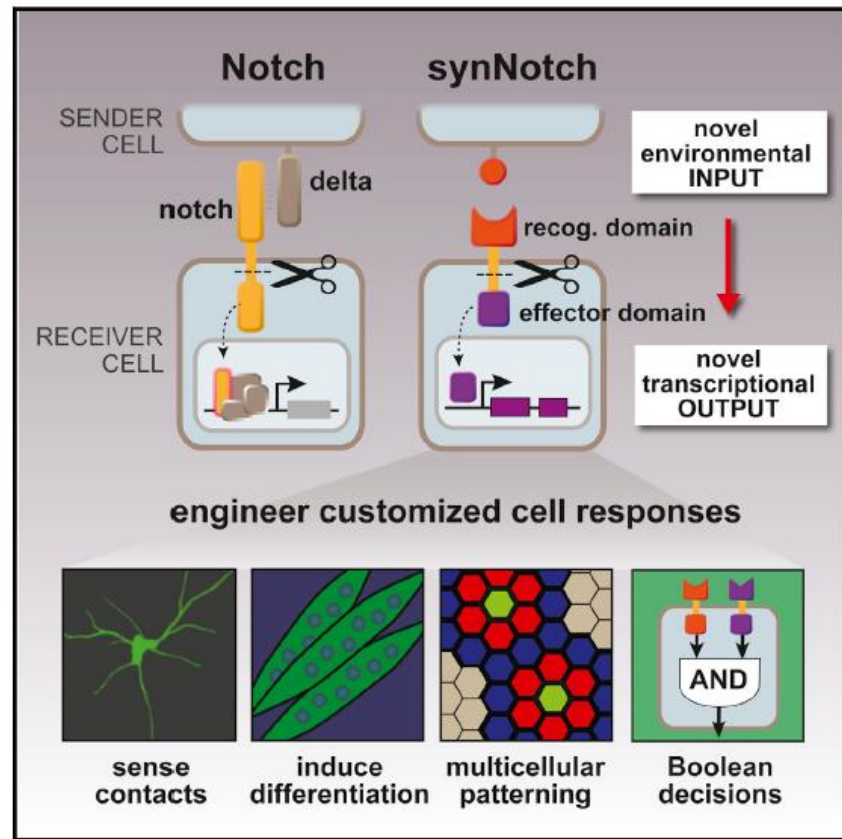


Image credit: Morsut et al., *Cell*, 2016

Drugs
Diagnostics
Devices

Drugs

- Possibilities:
 - Improving delivery
 - Improving therapeutic window

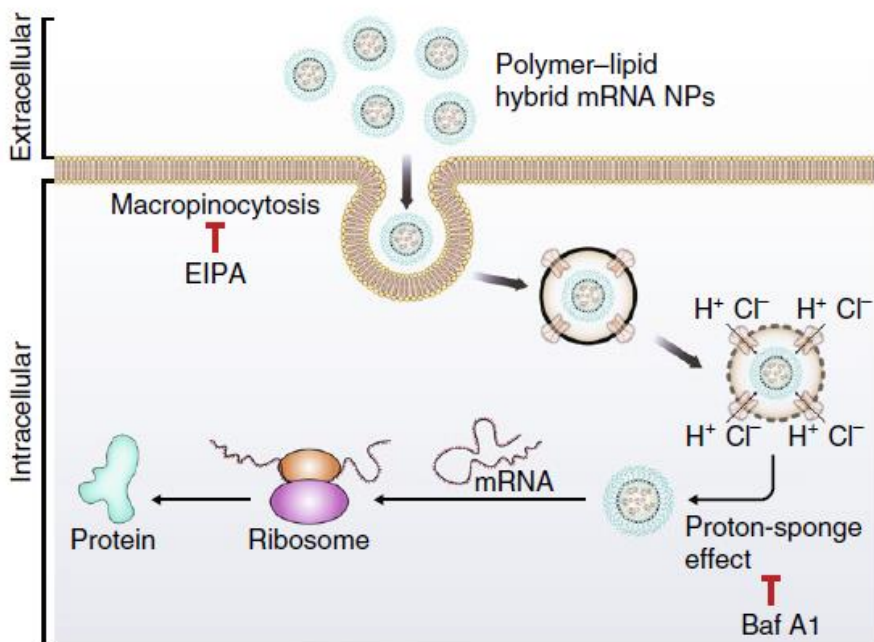
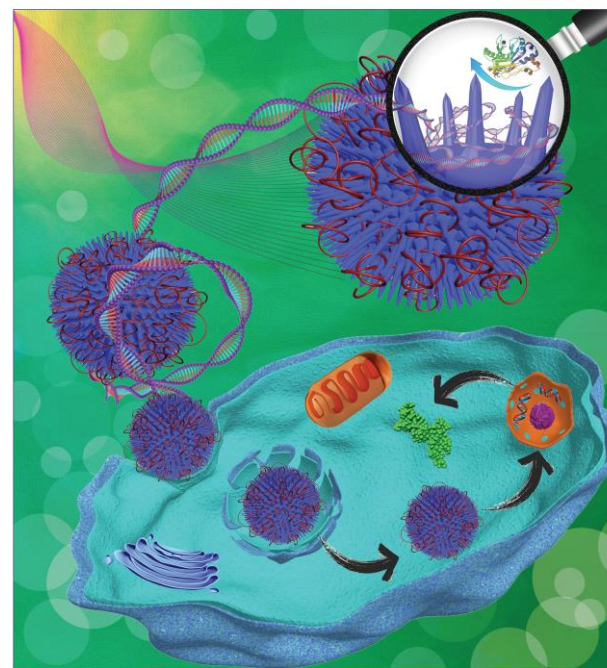


Image credit: Islam et al., *Nature Nanotechnology* 2018

December 20, 2017
Volume 139
Number 50
pubs.acs.org/JACS

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Image credit: *Journal of the American Chemical Society*

Drugs

- Possibilities:
 - Improving delivery
 - **Improving therapeutic window**

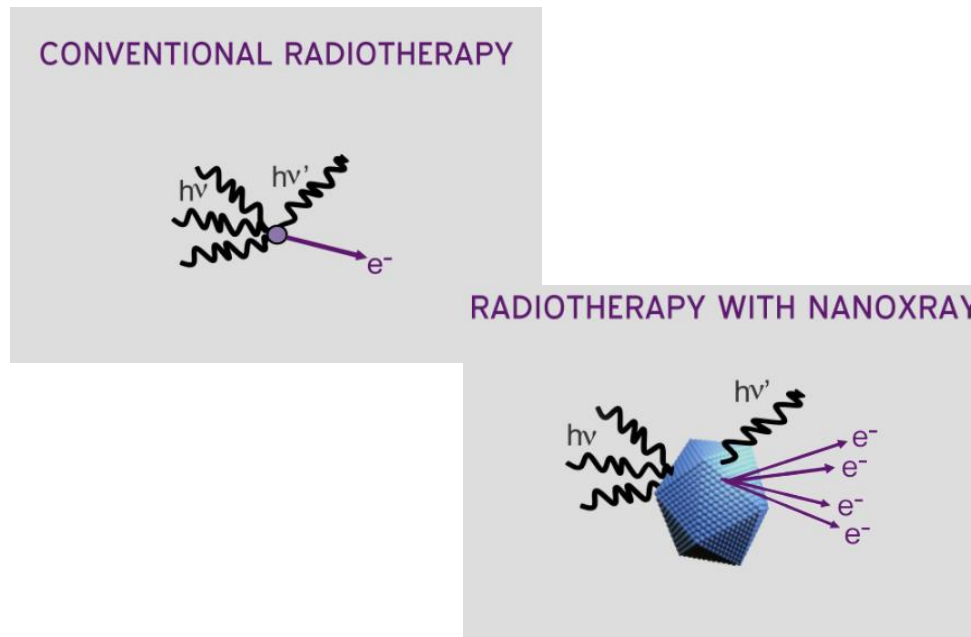


Image credit: Nanobiotix SA

Diagnostics

- Possibilities:
 - Moving from anatomical to molecular scale in vivo
 - Combining with therapies (“theranostics”) / multifunctional particles

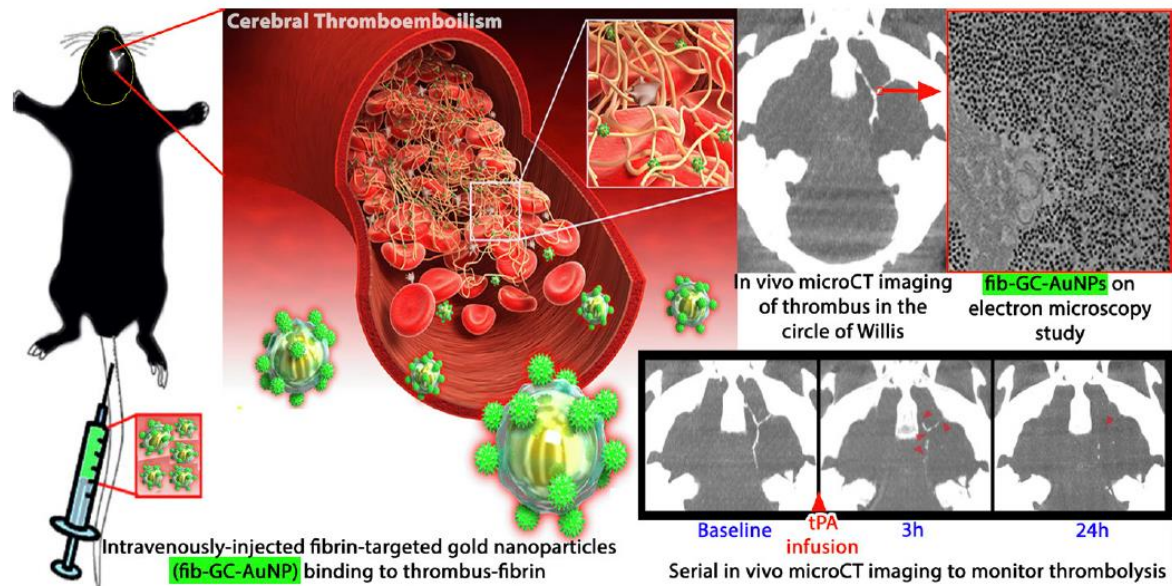


Image credit: Kim et al., *Stroke* 2016

Diagnostics

- Possibilities:
 - Moving from anatomical to molecular scale in vivo
 - **Combining with therapies (“theranostics”) / multifunctional particles**

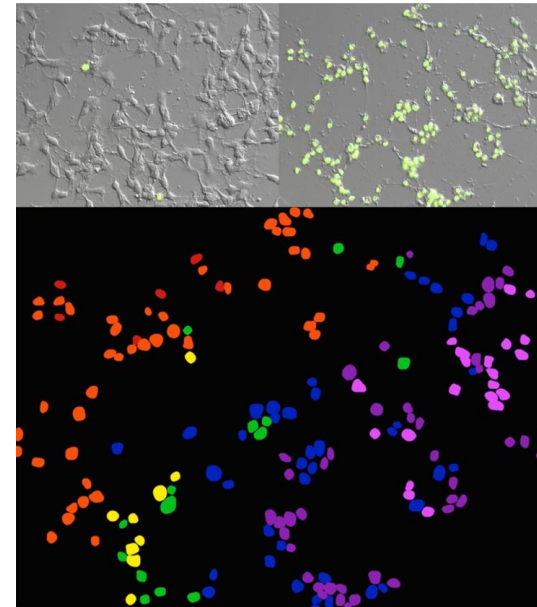
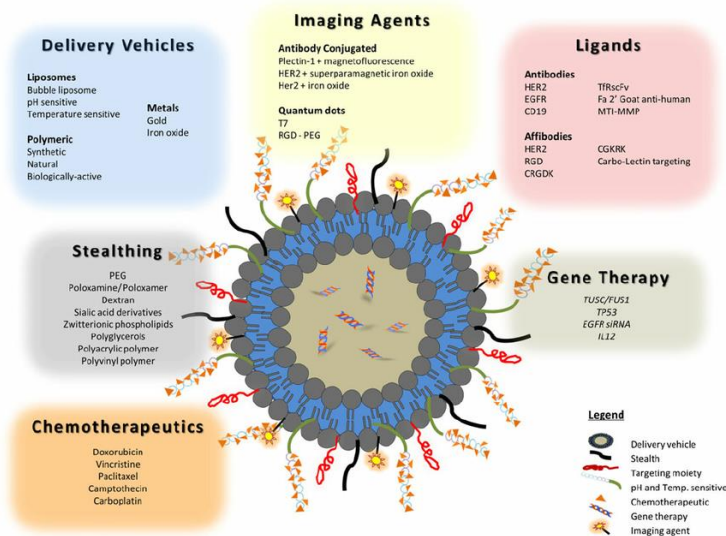


Image credit: Babu et al., *AAPS PharmSciTech* 2014

Image credit: National Cancer Institute \ MSK-Cornell
Center for Translation of Cancer Nanomedicine

Devices

- Possibilities:
 - **Noninvasive monitoring**
 - Implants

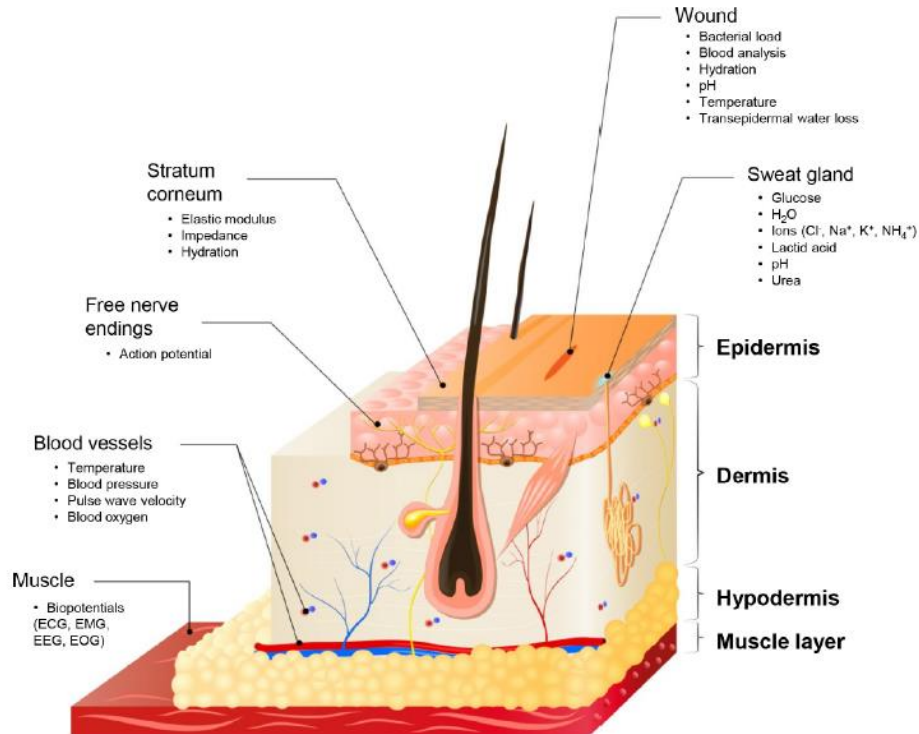


Image credit: Liu et al., *ACS Nano* 2017



Image credit: Liu et al., *ACS Nano* 2017

Devices

- **Possibilities:**
 - Noninvasive monitoring
 - **Implants**

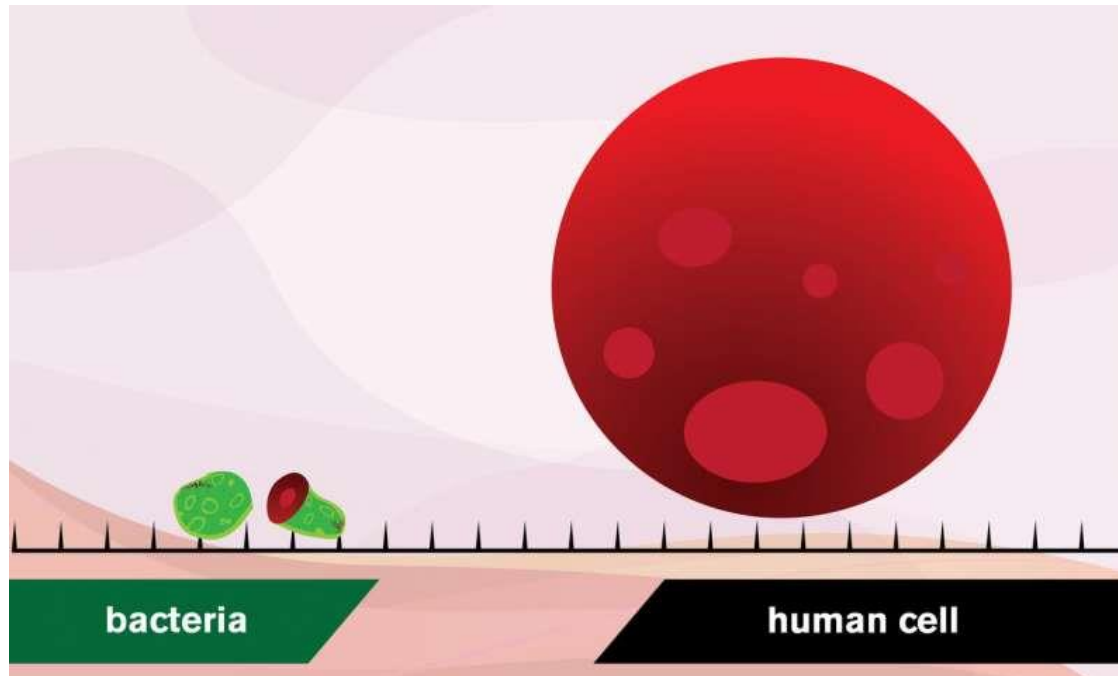


Image credit: Yen Strandqvist, Chalmers University of Technology

Risk

Risks:

- **To the patient**

Is it safe?

Where does it go?

How does it leave?

Does it all leave?

- **To the environment**

Where does it go after it's gone?

**Regulatory
Guidance**

Regulatory Guidance on Using Nanotechnology for Medical Devices

- Regulatory frameworks in various stages of development
- In many jurisdictions, few if any guidelines
- Standards often the only guides available to manufacturers

FDA/U.S.

- Early efforts to address nanotechnology, nanoscale materials
 - 2006 meetings



FDA/U.S.

- Guidances:
 - June 2014 agency-wide characterization guidance
 - December 2017 CDER guidance for nanoscale materials in drug products
 - Industry concerned about lack of specifics

Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology: Guida... 3 / 14

Contains Nonbinding Recommendations

Guidance for Industry
Considering Whether an FDA-Regulated Product Involves
the Application of Nanotechnology¹

This guidance represents the Food and Drug Administration's (FDA's or the Agency's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this guidance.

I. INTRODUCTION AND SCOPE

Nanotechnology is an emerging technology that can be used in a broad array of FDA-regulated products, including medical products (e.g. to increase bioavailability of a drug), foods (e.g., to improve food packaging) and cosmetics (e.g. to affect the look and feel of cosmetics). Materials

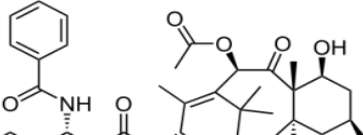
FDA/U.S.

- FDA approvals for nanotechnology
 - Drugs
 - Abraxane, approved in 2005, additional indications for use


Experimental Measurement and Computational Modeling of In Vivo Drug Dissolution for Accurate B... 3 / 10

Albumin Paclitaxel Nanoparticle (Abraxane) Shows Different Clinical Efficacy From Paclitaxel --- not BE

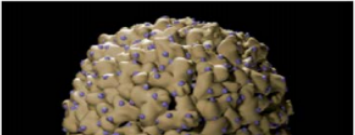
- **Paclitaxel indications**
 - Breast cancer, Ovarian cancer, non-small cell lung cancer, AIDS related sarcoma
- **Abraxane indications**
 - Metastatic breast cancer
 - After failure of combination chemotherapy for metastatic disease or relapse with 6 months of adjuvant chemotherapy
 - Locally advanced or metastatic non-small cell lung cancer
 - First line treatment in combination with carboplatin
 - Metastatic pancreatic cancer
 - First line therapy in combination of gemcitabine



Chemical structure of Paclitaxel

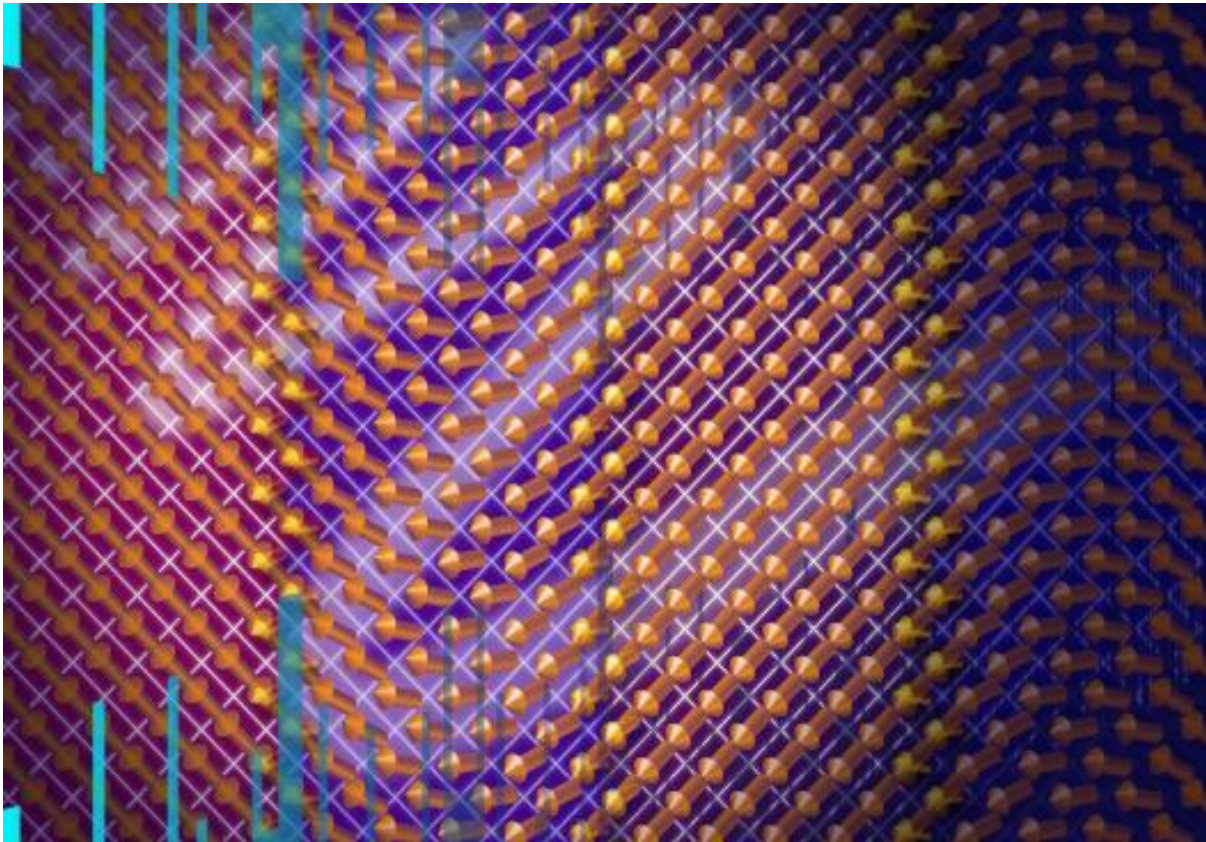


hydrophobic drug
Size : ~ 50-150 nm



FDA/U.S.

- FDA approvals for nanotechnology
 - Devices
 - Vallum's PEEK-Plus



FDA/U.S.

- FDA approvals for nanotechnology
 - Nanotechnology in Diagnostics
 - Verigene diagnostic by Nanosphere Inc./Luminex



510(k) Summary

The Summary for this 510(k) submission is submitted in accordance with the requirements of SMDA 1900 and CFR 807.92

510(k) Number:

K122514 Verigene[®] Gram-Positive Blood Culture Nucleic Acid Test (BC-GP)

Summary Preparation Date:

September 17, 2012

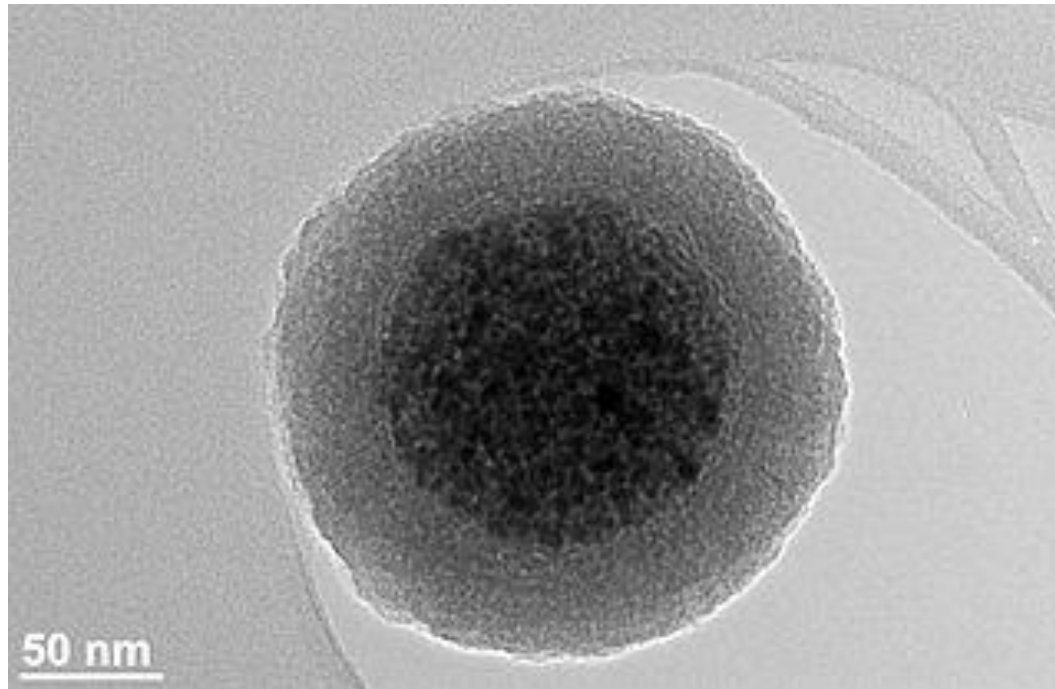
Submitted by:

Nanosphere, Inc.
4088 Commercial Avenue

SEP 19 2012

FDA/U.S.

- FDA approvals for nanotechnology
 - Drug-device combo in imaging
 - Endomagnetics' Magtrace/Sentimag for sentinel lymph nodes



FDA/U.S.

- FDA approvals for nanotechnology
 - Nanotechnology in interventional cardiology
 - Celonova PzF nanocoated stent for coronary arteries



FDA/U.S.

- FDA Standards adoption
 - ISO and ASTM standards



Standards-setting entities

- ASTM (formerly known as the American Society for Testing and Materials)
 - ASTM-E2490-09
 - ASTM-E2535-07
 - ASTM-E2865-12
 - ASTM 2859-11
- ISO
 - ISO/TS 14101
 - ISO 10993
 - ISO/TS 80004-6
 - ISO 29701

FDA/U.S.

- Other U.S.
 - National Nanotechnology Initiative
 - Funding and activities across several departments/agencies
 - NIOSH notification regarding silver nanoparticles in workplace exposure



National Nanotechnology Initiative

EMA/EU

- 2014 paper for risk assessment for devices with nanoscale materials
- MDRs address risks of nanoscale materials based on contact with body
- European Chemicals Agency/REACH



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

MHRA/U.K.

- MHRA's last definitive statement on nanotechnology was in 2009
- Agency said it will steer roughly parallel to EU on regulations generally



In conclusion...

- * FDA offers the most guidance regarding nanotech in medical devices
- * EU regulation focused largely on materials, safety
- * When in doubt, it's not location, location, location, but standards, standards, standards!



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