Матеріали в медицині: метали, кераміка, полімери. Європейське законодавство щодо застосування біоматеріалів

«Modern European trends in biomedical higher education: Bionanomaterials.» № 620717-EPP-1-2020-1-UA-EPPJMO-MODULE

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BIOMATERIALS

- “a systemically and pharmacologically inert substance designed for implantation within or incorporation with living systems”
- “a nonviable material used in a medical device, intended to interact with biological systems”
- “materials of synthetic as well as of natural origin in contact with tissue, blood, and biological fluids, and intended for use for prosthetic, diagnostic, therapeutic, and storage applications without adversely affecting the living organism and its components”
- “any substance (other than drugs) or combination of substances, synthetic or natural in origin, which can be used for any period of time, as a whole or as a part of a system which treats, augments, or replaces any tissue, organ, or function of the body”

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Some history

- There is evidence that sutures may have been used as long as 32,000 years ago (NATNEWS, 1983)
- 3000 B.C.: earliest report of a surgical suture (An ancient Egypt)
- Galen of Pergamon (circa 130–200 a.d.) described ligatures of gold wire.
- 900 A.D.: estimated year (from carbon dating) of the first dental implant found in Europe, which was found to have properly integrated bone
- 1829: H.S. Levert studies canine responses to implanted metals
- 1886: German doctor H. Hansmann is the first surgeon to use metal plates for internal fixation
- Glass contact lens made by Adolph Fick based on da Vinci's idea (1887)
- 1931: Boston surgeon Smith Peterson develops a metal cup for partial hip implants

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Some more history

- 1937 – PMMA was introduce in surgery
- 1939 – 1945: WWII spurs the development of many new materials and orthopaedic surgical techniques
- Dialysis machine made from cellulose membranes by Kolff (1943)
- First intraocular lens made from polymethyl methacrylate used by Kolff (1949)
- 1960- Polyethylene and stainless steel being used for hip implants
- In 1957, Dr. Willem Kolff and a team of scientists tested the artificial heart in animals
- In 1952 the first vessel prosthesis was successfully implanted in a human
- Coronary stents were developed in the mid-1980s
- 1980s – till now revolution in biomaterials

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Biomaterial requirements

- Technical functionality and mechanical properties tuned to the specific application
- Sufficient stability against physiological media
- Residue-free metabolization for biodegradable biomaterials
- High biocompatibility
- Non-allergenic
- Non-inflammatory
- Non-carcinogenic
- Simple processing
- Sterilizable without changes in form and composition
- Sufficiently long shelf-life

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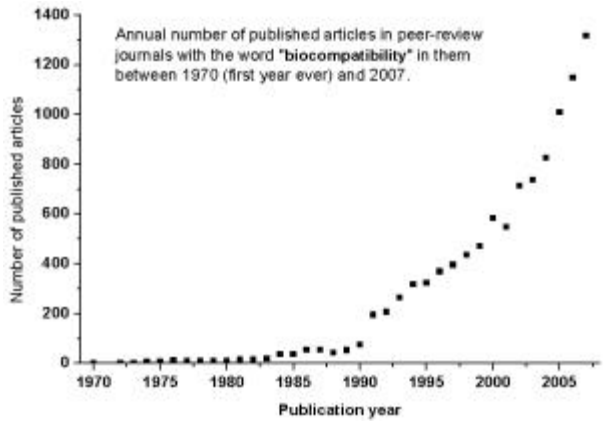
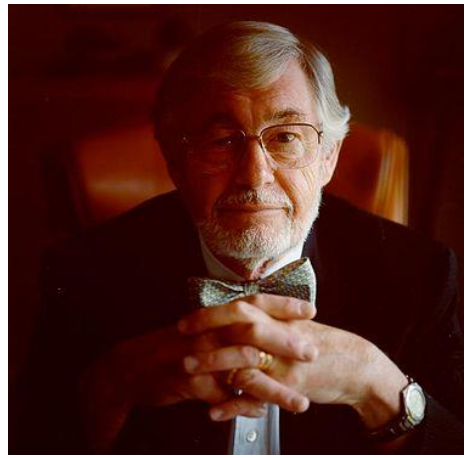
Biocompatibility

"Refers to the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient or beneficiary of that therapy, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimising the clinically relevant performance of that therapy"

First time refered

Homsy, Charles (1970). "Bio-Compatibility in selection of materials for implantation". *Journal of Biomedical Materials Research*. **4** (3): 341–356. doi:10.1002/jbm.820040306





Per-Ingvar Brånemark

Discovering of OSSEOINTEGRATION

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Biomaterial classification

Uses of Biomaterials

Problem Area	Examples
Replacement of diseased or damaged part	Artificial hip joint, kidney dialysis machine
Assist in healing	Sutures, bone plates, and screws
Improve function	Cardiac pacemaker, intraocular lens
Correct functional abnormality	Cardiac pacemaker
Correct cosmetic problem	Augmentation mammoplasty
Aid to diagnosis	Probes and catheters
Aid to treatment	Catheters, drains

Parida P. et al.

http://iaesjournal.com/online/index.php/IJAAS

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Biomaterial classification

Biomaterials in Organs

Organ	Examples
Heart	Cardiac pacemaker, artificial heart valve, total artificial heart, blood vessels
Lung	Oxygenator machine
Eye	Contact lens, intraocular lens
Ear	Artificial stapes, cochlea implant
Bone	Bone plate, intramedullary rod
Kidney	Catheters, stent, Kidney dialysis machine
Bladder	Catheter and stent

Parida P. et al.

http://iaesjournal.com/online/index.php/IJAAS

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Biomaterial classification

Biomaterials in Body Systems

System	Examples
Skeletal	Bone plate, total joint replacements
Muscular	Sutures, muscle stimulator
Nervous	Hydrocephalus drain, cardiac pacemaker, nerve stimulator
Endocrine	Microencapsulated pancreatic islet cells
Reproductive	Augmentation mammoplasty, other cosmetic replacements
...	

Parida P. et al.

http://iaesjournal.com/online/index.php/IJAAS

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What materials used for….

- Metals
- Ceramic
- Polymers
- Composites
- Nanomaterials

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Metals

Properties

- High strength
- Inert nature
- Relatively easy to produce
- Biocompatibility
- Easy to modify

What metals used?

- Titanium
- Tantalum
- Stainless steel
- Vanadium
- Zirconium
- Iron
- Zink
- Magnesium

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Examples

Conventional

Personalized

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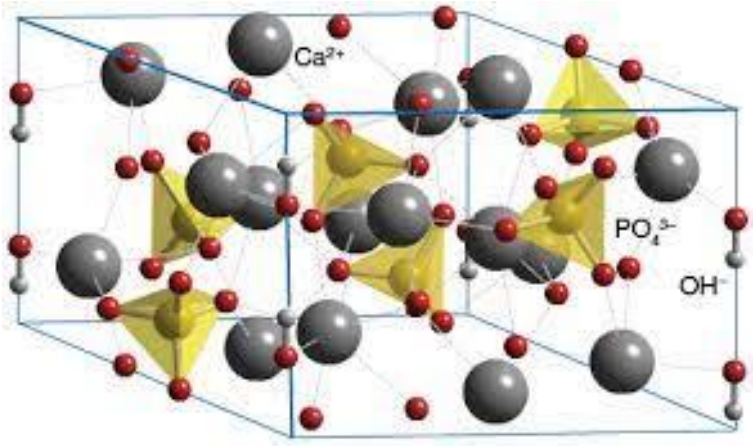
Ceramic

- A **ceramic** is an inorganic non-metallic solid made up of either metal or non-metal compounds that have been shaped and then hardened by heating to high temperatures.



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Ceramic types

Type	Example
Non-absorbable (inert)	Alumina, zirconia, silicone nitrides, and carbons
Bioactive or surface reactive (semi-inert)	Glass ceramics and dense hydroxyapatites
Biodegradable or resorbable (non-inert)	Calcium phosphates and calcium aluminates

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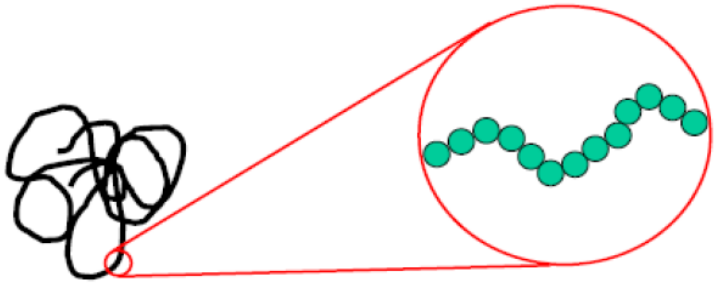
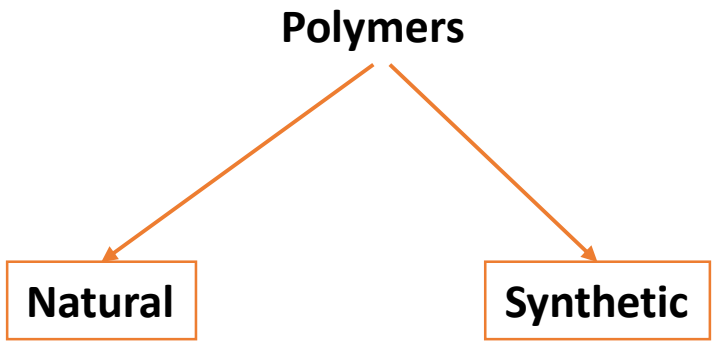
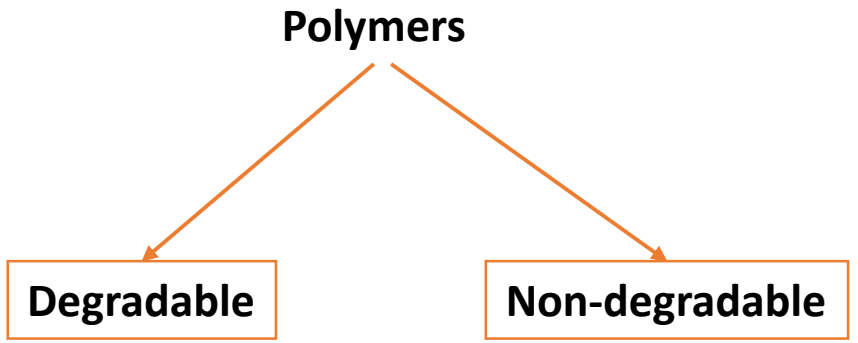
Polymers

- Macromolecule consisting of repetition units







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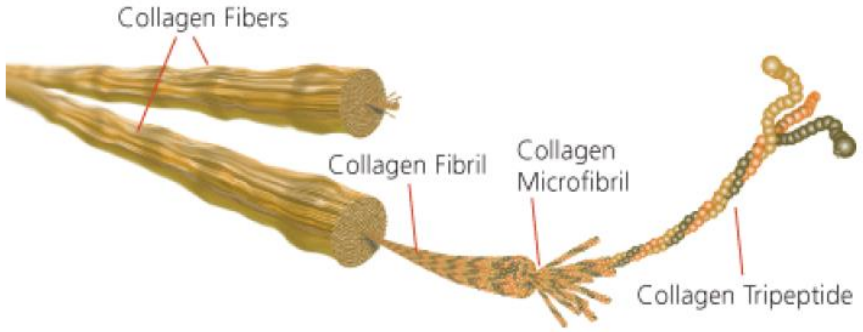
Examples of natural polymers

- **Polyesters** (Polylactic acid)
- **Proteins** (silk, soy protein)
- **Polysaccharides** (gelatin, chitosan, cellulose)
- **Polyphenols** (lignin, tannin)
- **Lipids** (Waxes)
- **Specialty polymers** (Natural rubber, PDA)



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Application

- Cardiovascular and general surgery: Implants (bladder, skin, heart)
- Dental Applications (Implants, Fillers,…)
- Surgery
- Sensors, biochips, implants, microoptic devices
- Contact lenses
- Drug transporter
- Tissue engineering
- …

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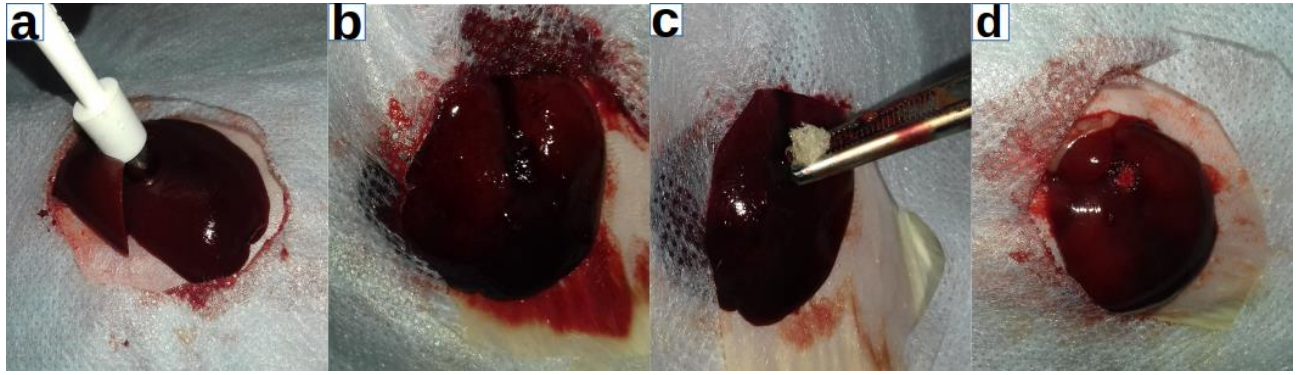
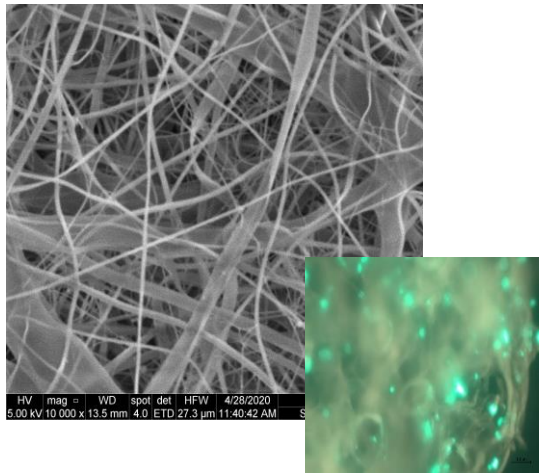
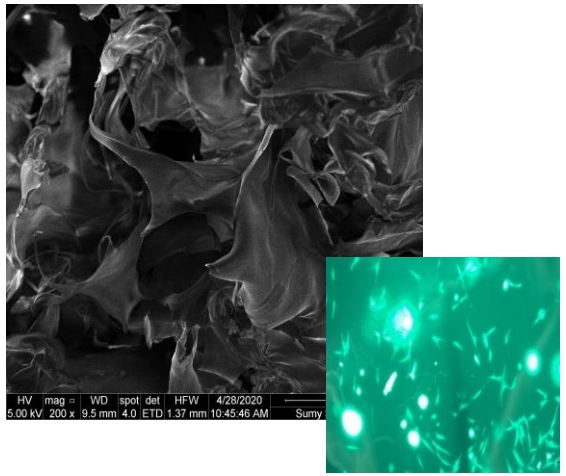
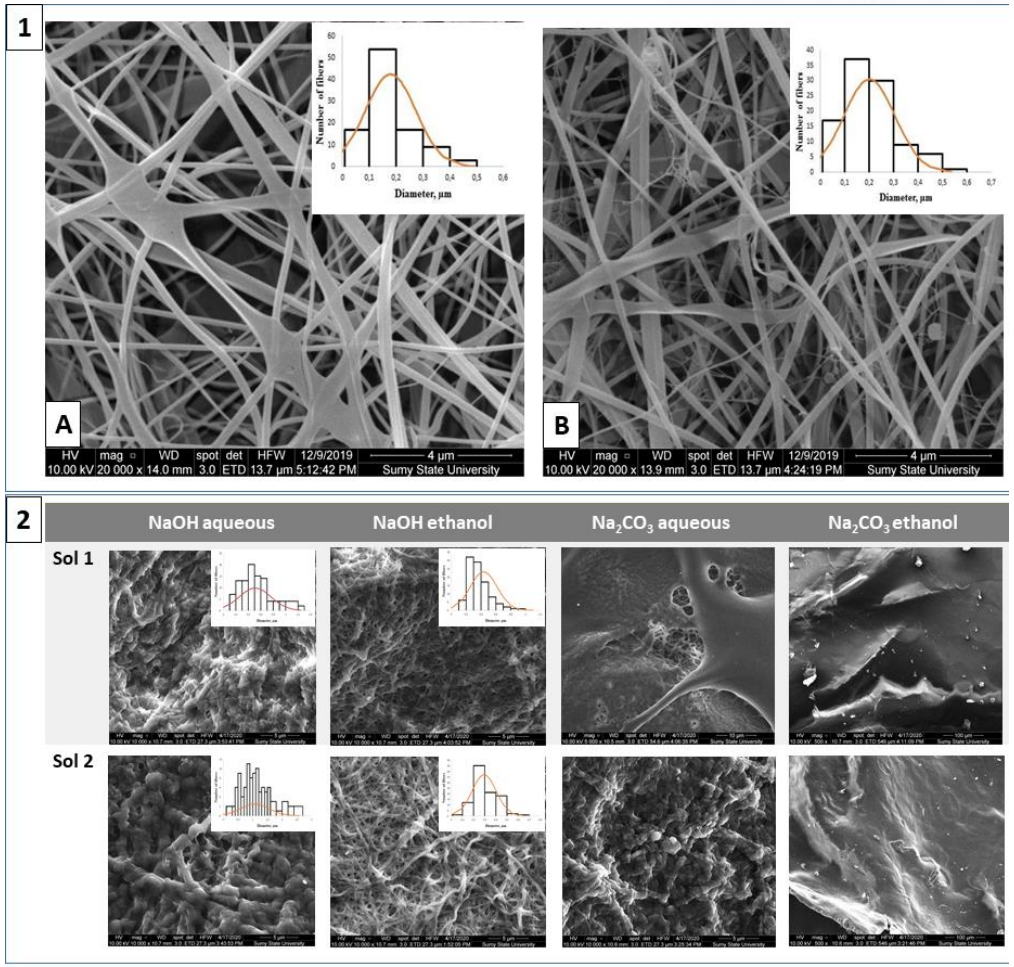
Our results



Procedure of punch biopsy liver trauma (a), liver bleeding (b), hemostatic application (c) and stopped bleeding (d).







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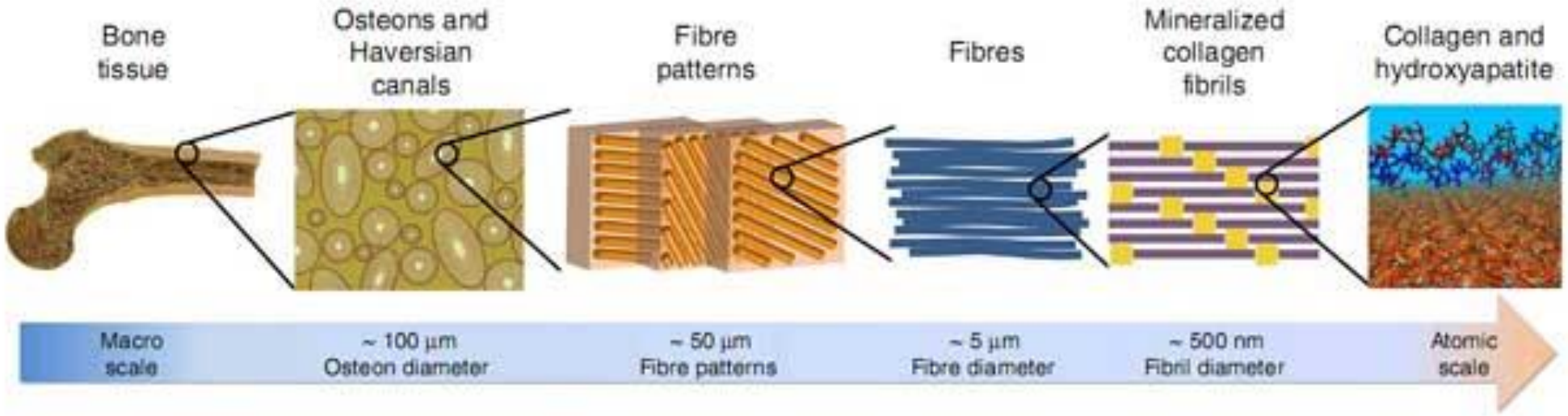
Composites

- Materials, contain more then one phase or materials



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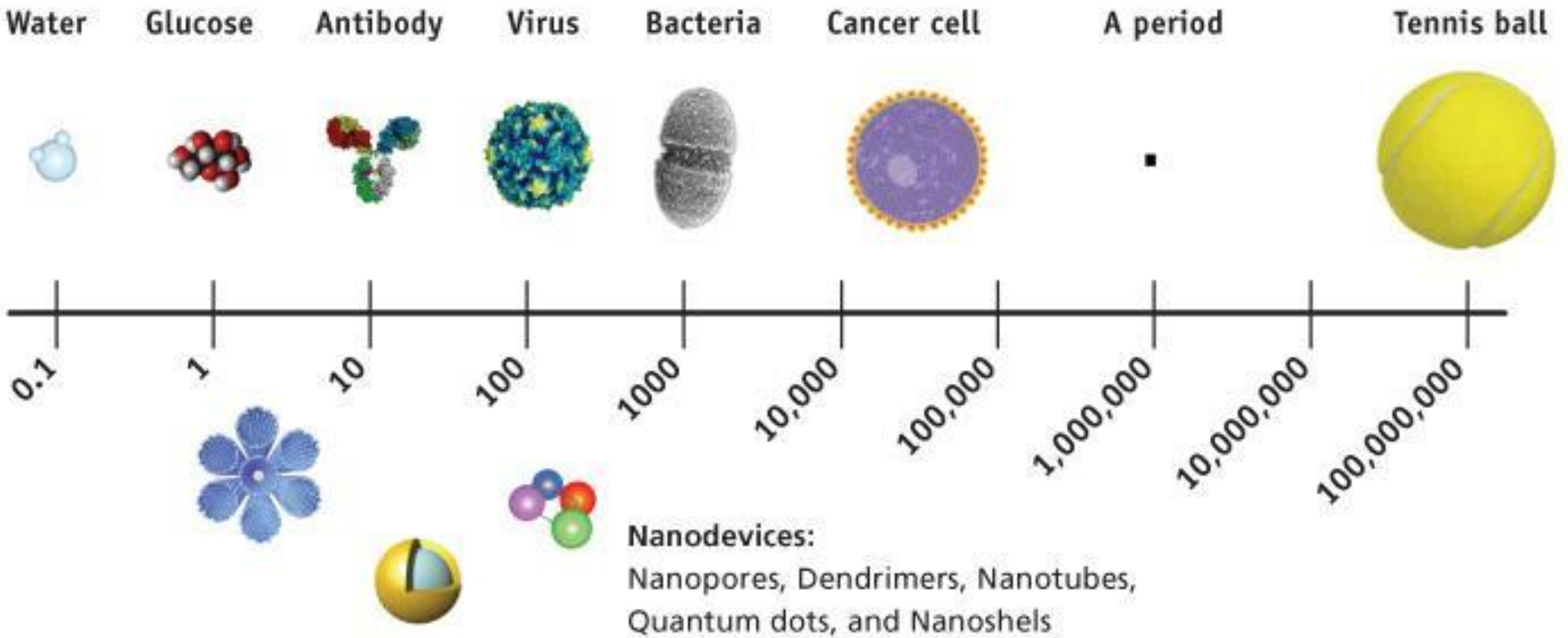
Nanomaterials



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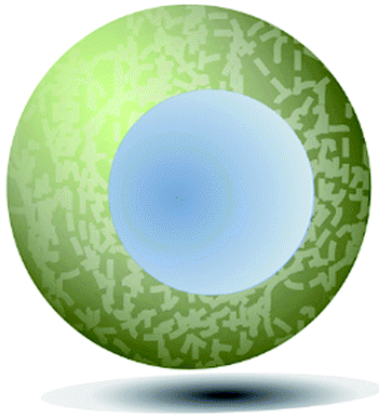
Examples of Nanomaterials

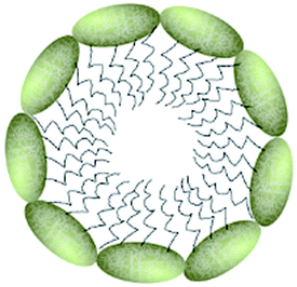
Organic nanoparticles

Polymeric nanosphere

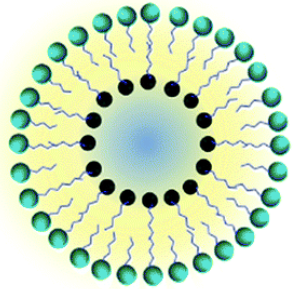
Polymeric nanocapsule



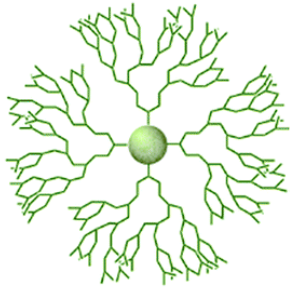
Polymeric micelle



Liposome



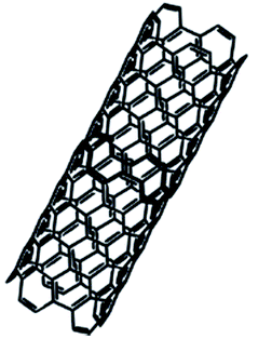
Dendrimer



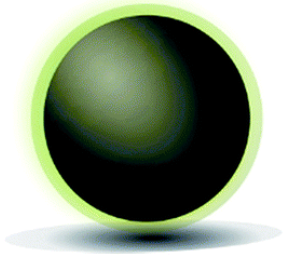
Inorganic nanoparticles

Mesoporous silica nanoparticle

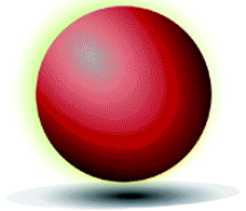
Carbon nanotube



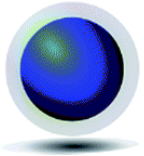
Iron oxide nanoparticle



Gold nanoparticle



Quantum dot



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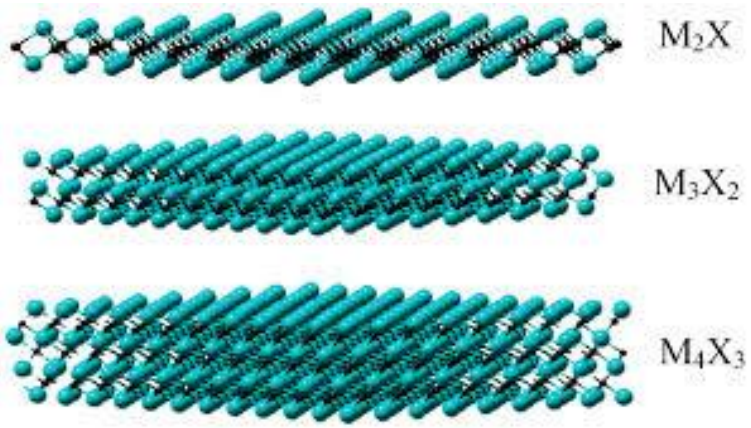
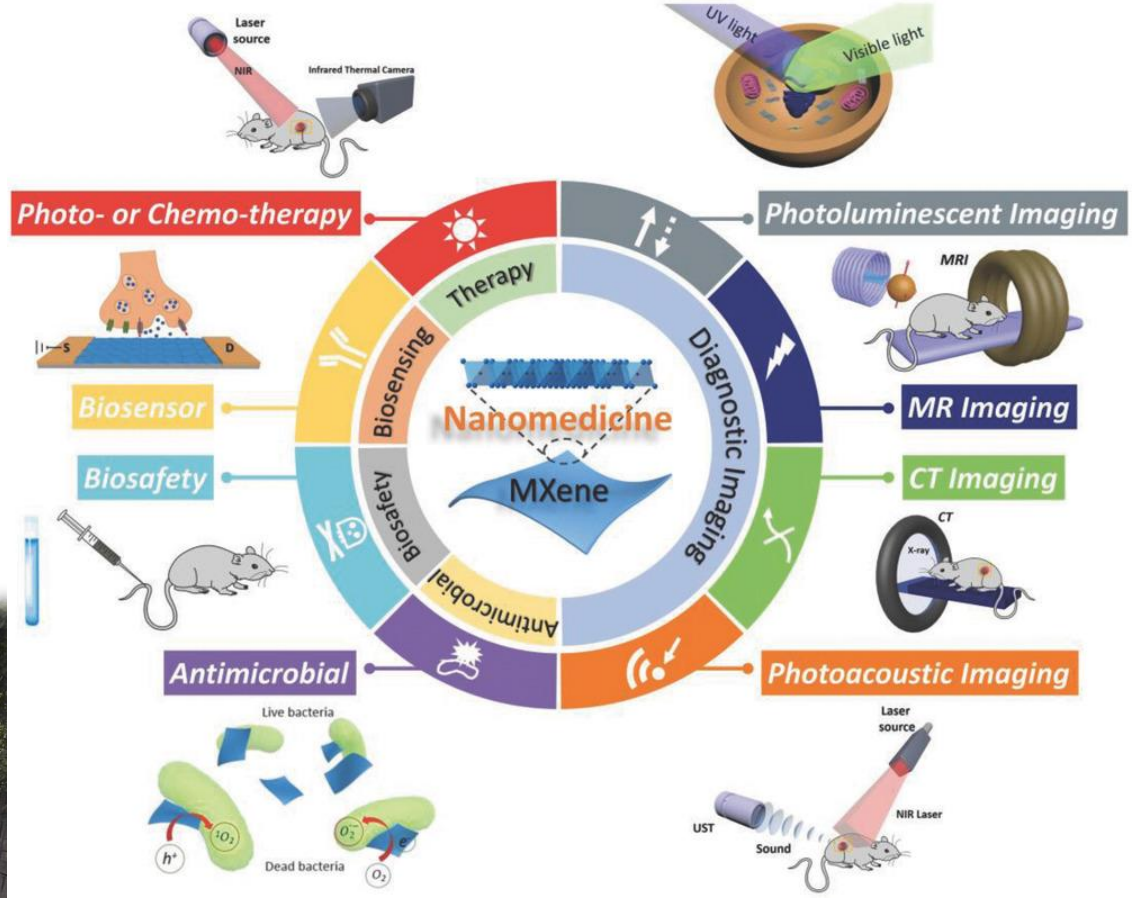
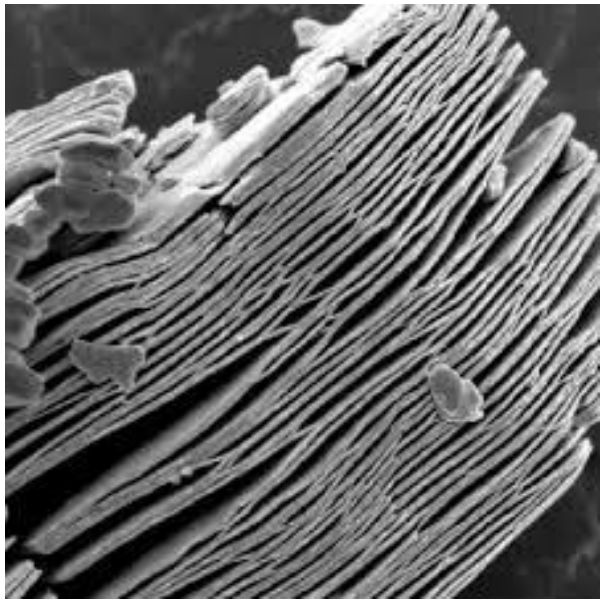
2D nanolaminates (MXene, as example)







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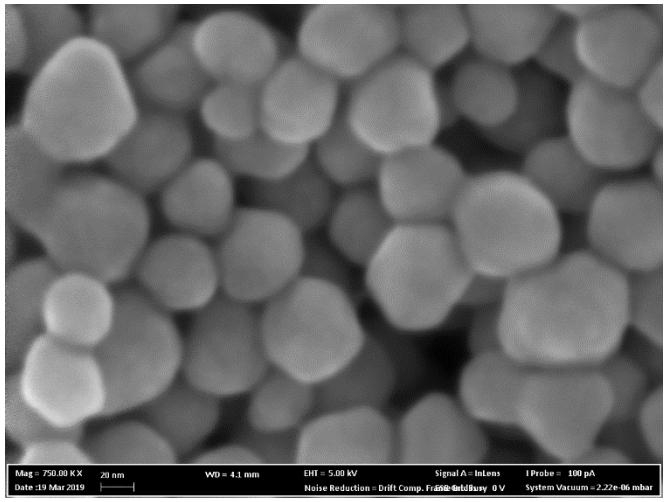
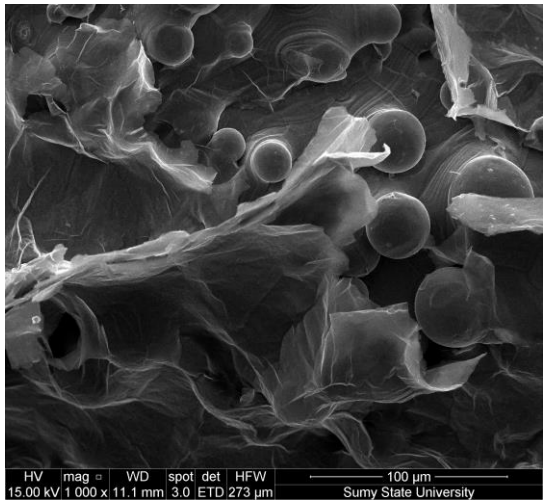
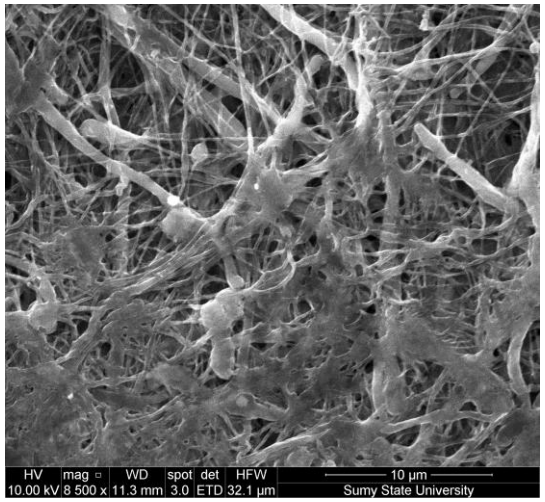
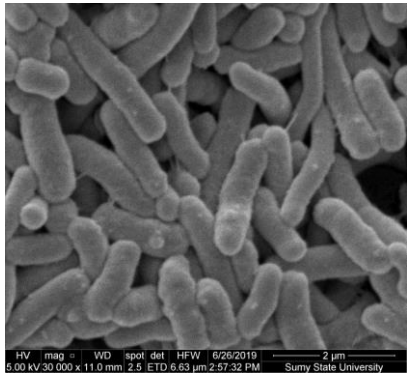
Our example

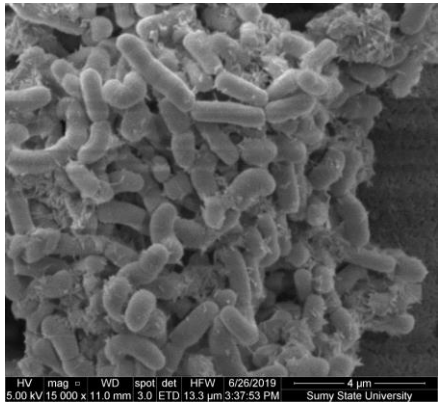




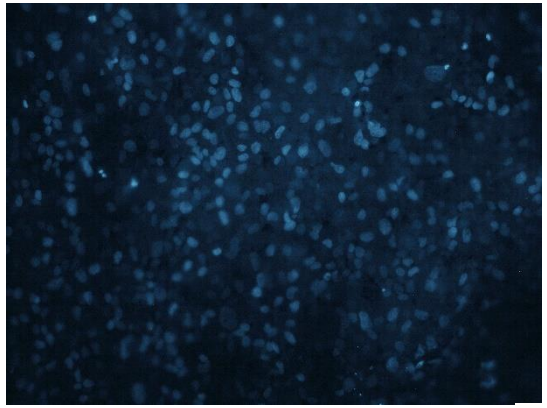


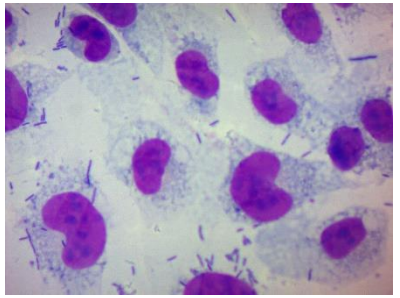
Silver Nanoparticles, made in SumDU

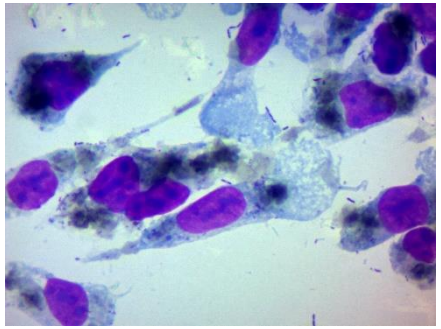




MXene-coated 3D metal and PCL scaffold







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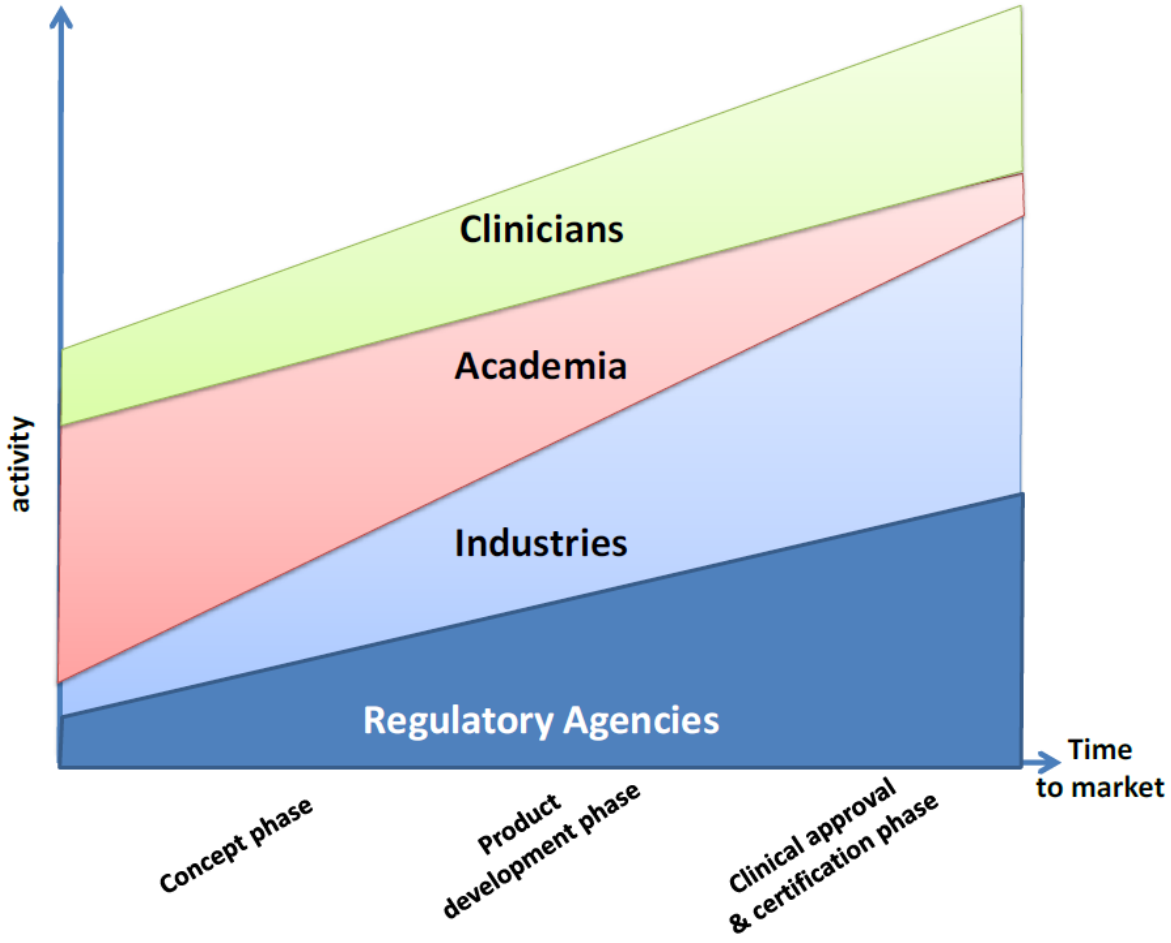
Biomaterials: European Regulatory and Legal Aspects

Technology Readiness Levels as applicable to Healthcare

Level		
1	Basic Principles Observed and Reported	Potential scientific application to defined problems is articulated.
2	Technology Concept and/or Application Formulated	Hypothesis(es) generated. Research plans and/or protocols developed, peer reviewed, and approved.
3	Analytical and Experimental Critical Function and/or Characteristic Proof of Concept	Basic research, data collection, and analysis. First hypotheses tested
4	Validation in Laboratory/Field Environment	Non GxP laboratory research to refine hypothesis
5	Component and/or Breadboard Validation in a Relevant (Operating) Environment	Intense period of nonclinical and pre-clinical GxP research studies involving
6	Prototype Demonstration in a Realistic (Operating) Environment or Context	Phase I Clinical Trials
7	System Prototype Demonstration in an Operational Environment or Context	Phase II Clinical Trials
8	Actual System Completed and Qualified through Test and Demonstration	Phase III Clinical Trials
9	Actual System Operationally Proven through Successful Mission Operations	Post Marketing Studies

Involvement of the various stakeholders in in biomaterials research



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ISO 10993 standard

- ISO 10993-1:2018 Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process
- ISO 10993-2:2006 Biological evaluation of medical devices Part 2: Animal welfare requirements
- ISO 10993-3:2014 Biological evaluation of medical devices Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
- ISO 10993-4:2017 Biological evaluation of medical devices Part 4: Selection of tests for interactions with blood
- ISO 10993-5:2009 Biological evaluation of medical devices Part 5: Tests for in vitro cytotoxicity.
- ISO 10993-6:2016 Biological evaluation of medical devices Part 6: Tests for local effects after implantation
- ISO 10993-7:2008 Biological evaluation of medical devices Part 7: Ethylene oxide sterilization residuals
- ISO 10993-8:2001 Biological evaluation of medical devices Part 8: Selection of reference materials (withdrawn)
- ISO 10993-9:2010 Biological evaluation of medical devices Part 9: Framework for identification and quantification of potential degradation products
- ISO 10993-10:2013 Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization

ISO 10993 standard

- ISO 10993-23:2021 Biological evaluation of medical devices Part 23: Tests for irritation
- ISO 10993-11:2018 Biological evaluation of medical devices Part 11: Tests for systemic toxicity
- ISO 10993-12:2012 Biological evaluation of medical devices Part 12: Sample preparation and reference materials (available in English only)
- ISO 10993-13:2010 Biological evaluation of medical devices Part 13: Identification and quantification of degradation products from polymeric medical devices
- ISO 10993-14:2009 Biological evaluation of medical devices Part 14: Identification and quantification of degradation products from ceramics
- ISO 10993-15:2009 Biological evaluation of medical devices Part 15: Identification and quantification of degradation products from metals and alloys
- ISO 10993-16:2018 Biological evaluation of medical devices Part 16: Toxicokinetic study design for degradation products and leachables
- ISO 10993-17:2009 Biological evaluation of medical devices Part 17: Establishment of allowable limits for leachable substances
- ISO 10993-18:2020 Biological evaluation of medical devices Part 18: Chemical characterization of medical device materials within a risk management process
- ISO/TS 10993-19:2006 Biological evaluation of medical devices Part 19: Physico-chemical, morphological and topographical characterization of materials
- ISO/TS 10993-20:2006 Biological evaluation of medical devices Part 20: Principles and methods for immunotoxicology testing of medical devices
- ISO/TR 10993-22:2017 Biological evaluation of medical devices Part 22: Guidance on nanomaterials

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СумДУ

EUBiomt

BRC
BIOMEDICAL RESEARCH CENTRE

to be continued...

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