



Regulatory Assessment of New Bioresorbable Scaffolds: PMDA Point of View



Pharmaceuticals and Medical Devices Agency (PMDA)

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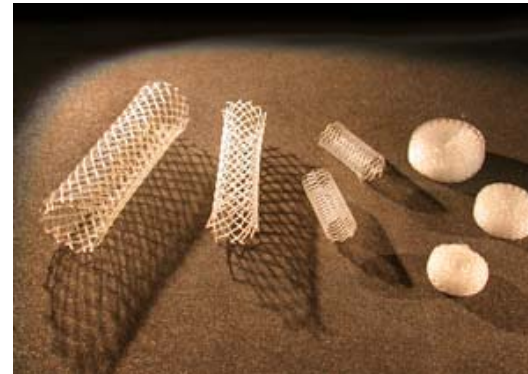
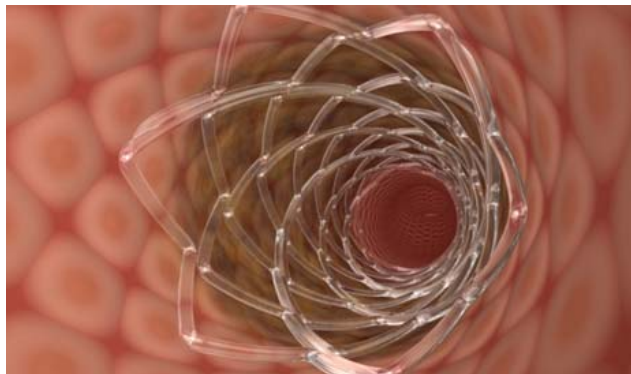
Today`s Agenda

- The purpose of development
- Points to consider in review process
~non-clinical part~
- Requirement for first in human
- Points to consider in review process
~clinical part~



What is the purpose of development?


- What is expected in utilization of this bioresorbable material?
- What characteristics/performance are anticipated in the design with the degradation/decomposition behavior of this bioresorbable material?





Points to consider in review process – non-clinical part

Additional items besides general stent requirements	Bioresorbable scaffold
Polymer characterization	Necessary
Mechanism of degradation	Necessary
Absorption profile	Necessary
Mechanical property	Necessary
Drug elution profile	Necessary
Safety of intermediate products	Necessary
Bench test	Determine the potential of aging change in addition to general performance testing
Animal study	Determine the potential of aging change during the polymer absorption period in addition to general testing



What Bench Test Should be Considered for Bioresorbable scaffolds?

- Characterization of polymer or metal
 - Absorption profile
 - Mechanism
 - Characterization of intermediate product
- General requirements for intravascular stent products to be marketed in Japan
 - Compliance with the MHLW notification regarding coronary stent products
 - Stent with full absorption characteristics needs sequential investigation with considerations of absorption behavior
 - Maintain mechanical strength while it is needed (until complete endothelialization)
- (Requirements relevant to drug elution)

Other related requirements

- Stability and durability of materials for device
- Biocompatibility of materials (including intermediate products)
- Evaluation with animal model
 - Coronary artery: Implant test in swine (pig) coronary arteries
 - Other arteries: Appropriate animal model with rationale for the selection of that model the study
- non-clinical evaluation to determine if the device meets its purpose of development

What are the requirements for a FIH

1. Safety for human use should be ensured based on non-clinical study.
2. Need to conduct FIH study with patient safety.
3. Following items should be confirmed in the pilot study
 - ✓ Safety for human use (deliverability, mechanical strength during endothelialization or reintervention)
 - ✓ Performance (success rate of procedure, performance in chronic phase, etc.)

The pivotal study should be designed based on these results as well as the clinical positioning of bioresorbable scaffolds.





Points to consider in review process –clinical part

1. Subject patients
 - ✓ similar population to existing DES trials?
2. Control arm
 - ✓ if the population is comparable, comparison to DES arm appropriate ?
3. Goal of the clinical trial
 - ✓ Determine superiority or non-inferiority to DES arm?
4. Primary endpoints
 - ✓ Clinical endpoints (e.g. TVF) ?
 - ✓ When should it be evaluated?
5. Other evaluation
 - ✓ Long term benefit (uncaged artery? Normalization of endothelial function?)



Points to consider in review process – clinical part

Important items

- Safety (in procedure, in acute to chronic phase, re-intervention before endothelialization, long-term effect)
- What to evaluate as the secondary endpoints (endothelialization of the target vessel? Efficacy and safety when bailout option is exercised? Compatibility with BMS or DES?)
- Duration of antiplatelet therapy? How to establish sufficient timeframe?
- Additional matters, (e.g. ease of deliverability or retreatment)



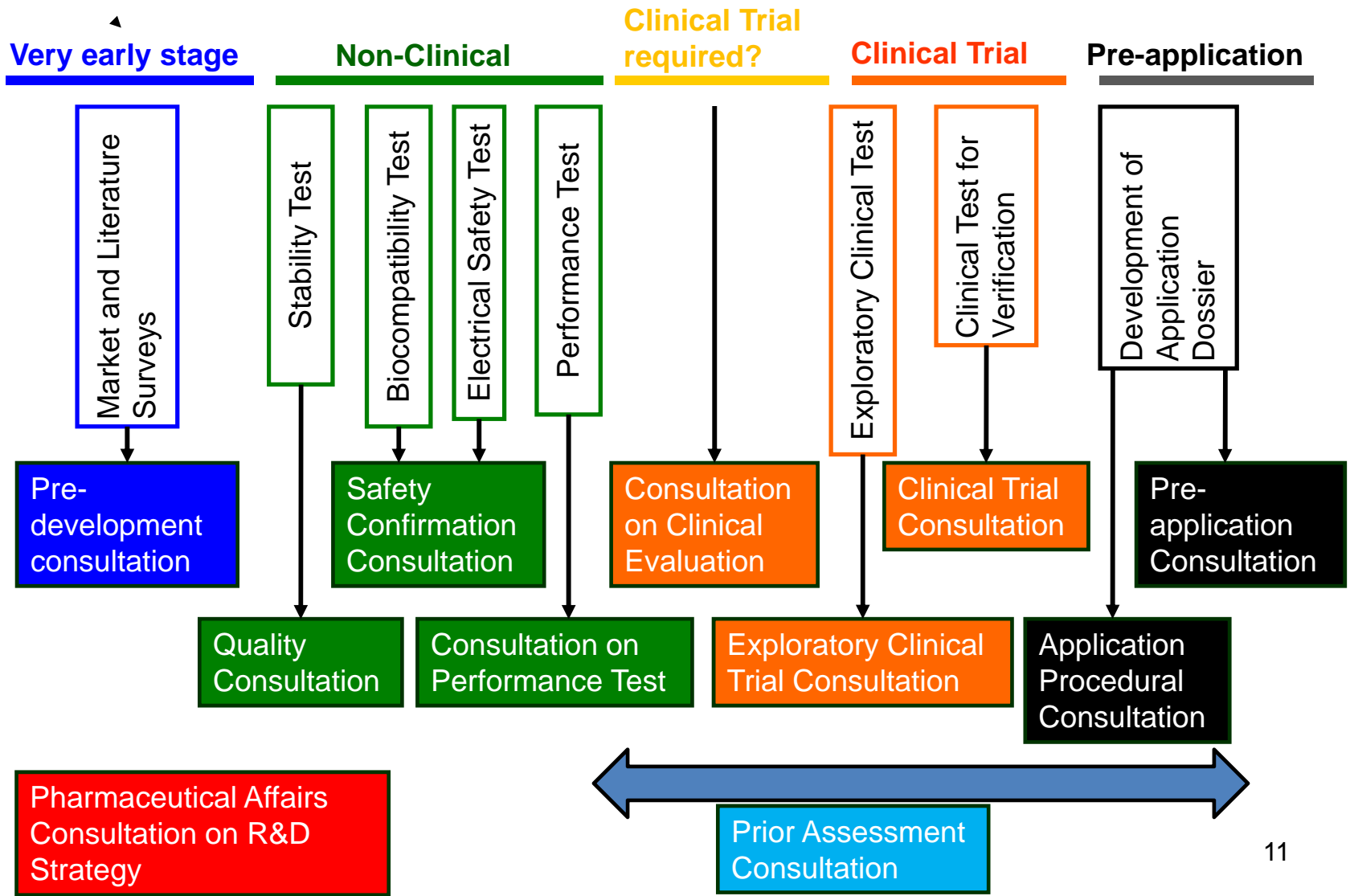
Conclusion :bioresorbable device

For streamlined development:

- Ensure safety
- Conduct small feasibility study
- Subsequently, utilize the results for the protocol design of pivotal study

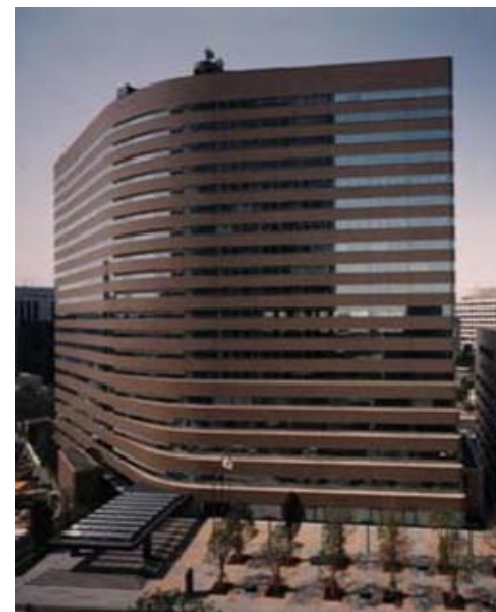
Contact PMDA through consultations from early development stage.

PMDA's Consultation Menu



PMDA, Japan

**If you have any questions,
Please contact us
Thank you!**



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