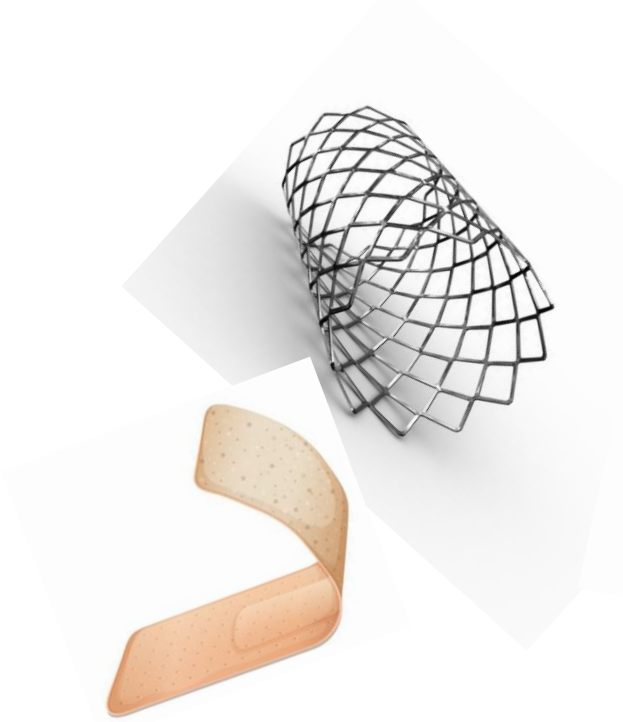
Disclaimer

This presentation is based on information available as of today and prepared to my best
knowledge as subject matter expert.

This presentation presents my personal understanding of the medical device requirements
in Europe and is not necessarily reflecting the view of TÜV SÜD PS.

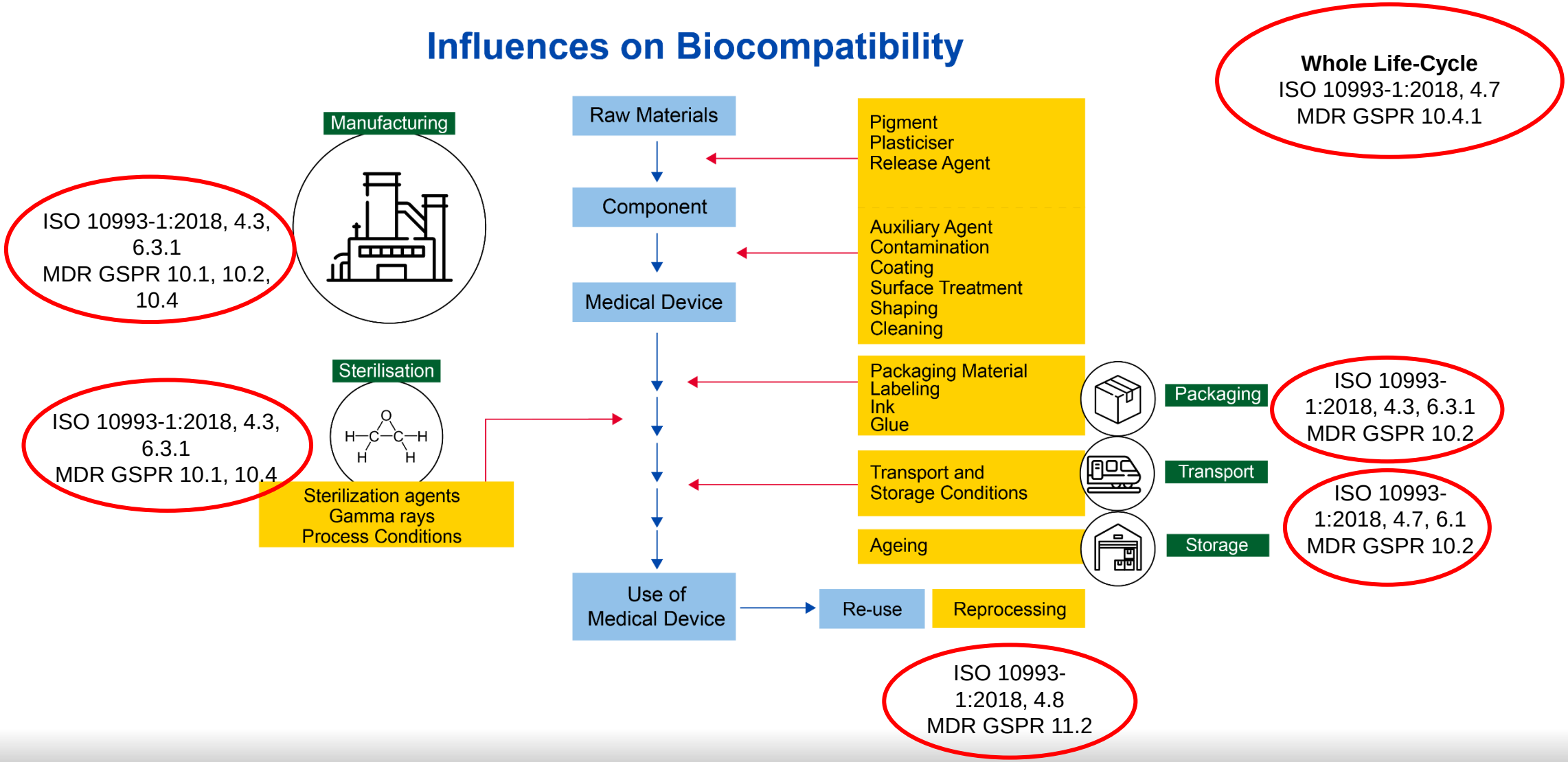
Impact of Packaging Materials on the Biological Safety of a Medical Device

Influence and depth of evaluation depends on device type (liquid vs. solid) and packaging material (polymer, glass, ...)

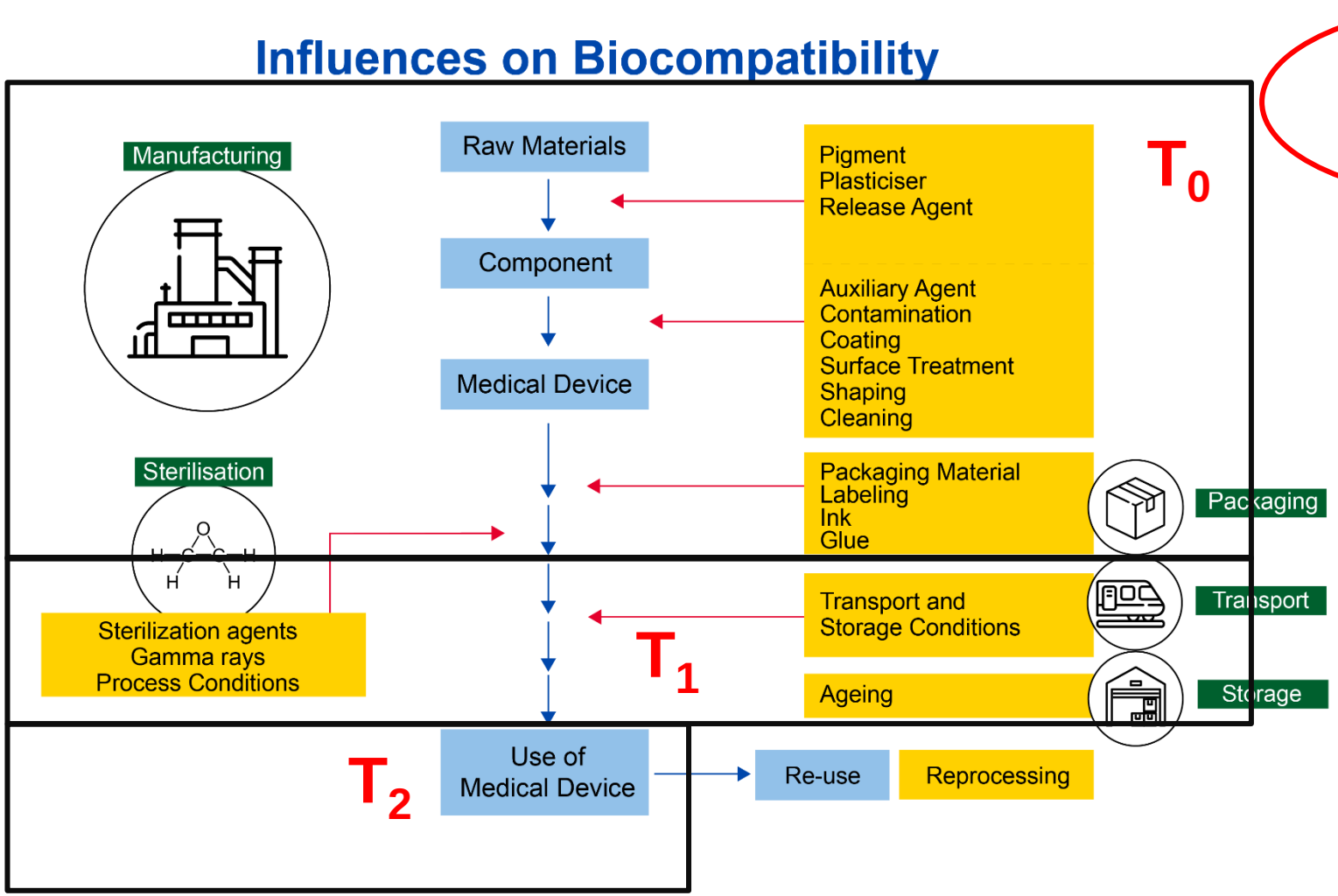


Usually, a solid deivce is less likely to interact with the packaging materials than a device composed of a semi-solid or liquid material

Potential Impacts on Biological Safety



Different Time Points in the Life-Cycle of a Medical Device



Whole Life-Cycle
ISO 10993-1:2018, 4.7

T_0 – Manufacturing Process, Packaging, Sterilization

- Raw materials
- Processing aids
- Cleaning agents or contaminations
- Surface treatment
- Transfer of contaminants
- Transfer/migration from glue, ink, label, etc.
- Transfer of packaging migrants
- Material alterations due to sterilization conditions

Endpoint-specific risk-assessment based on chemical and biological data

T_1 – End of Shelf-Life/Impact of Transport and Storage

- Transfer of packaging contaminants, glue, ink
- Transfer of packaging migrants
- Material alterations due to storage/transport conditions (reaction of substances or degradation/corrosion)

T_1 – End of Shelf-Life/Impact of Transport and Storage

Potential impact of Packaging Materials that come in contact with the Medical Device (primary packaging materials) on the physical, chemical, or biological properties must be evaluated, considering:

- Materials of the device
- Packaging Materials
- Usually, a solid device is less likely to interact with the packaging materials than a device composed of a semi-solid or liquid material

T_1 – Material Data from Packaging Materials

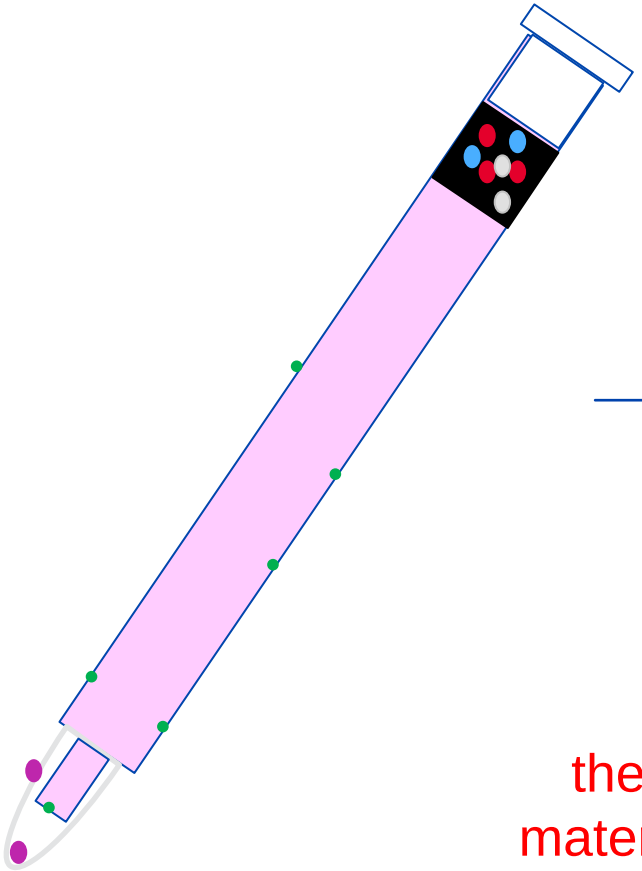
- can be helpful in order to adress the risk of migration of substances from the packaging materials to the device under assessment
- **USP-testing** performed with packaging materials are usually **not acceptable** to adress this risk, usually the following gaps appear:
  - testing is typically conducted on raw materials rather than final products
  - extraction conditions typically do not represent whole shelf life
  - potential interactions with the device are not adressed

  see also ISO 10993-1:2018, 6.2

T_1 – Example Liquid Device

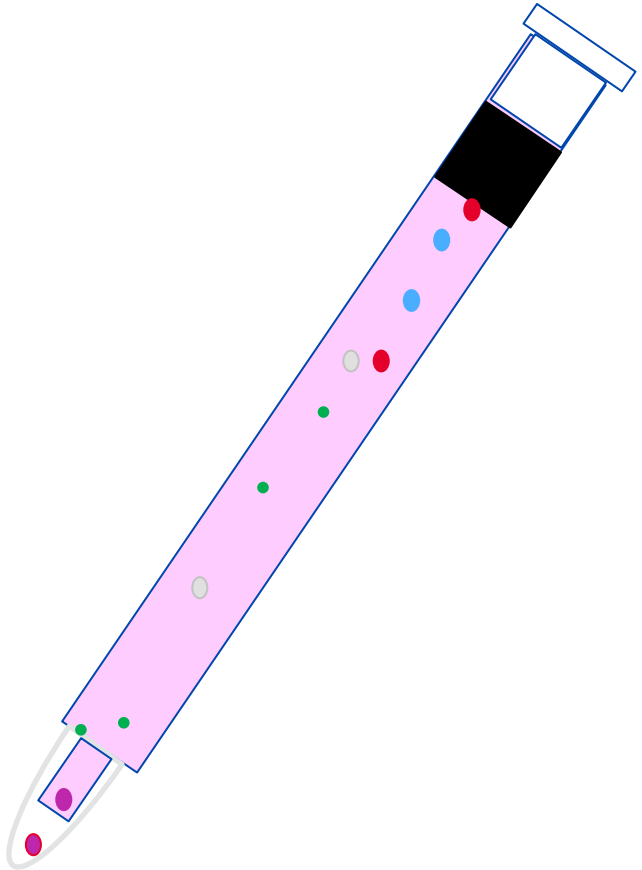
- Worst case with regard to potential leachables from primary packaging materials
- Leaching takes place during the complete shelf-life

T_1 – Example Liquid Device



shelf life

e.g. 2 years @ RT



theoretical assumptions based on material data might not be sufficient to adress the potential toxicological risk…

T_1 – Example Liquid Device

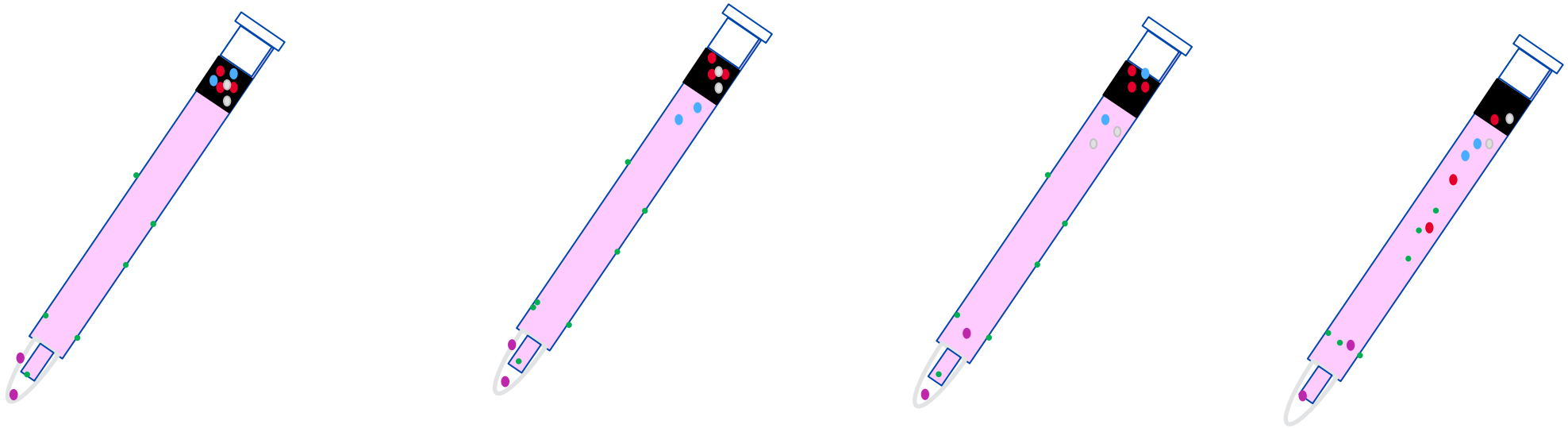
…but chemical analysis of the device after accelerated/real-time aging for this kind of devices often technically not feasible

Example: Chemical analytical testing and toxicological risk assessment of the packaging materials

T_1 – Example Liquid Device

Extraction Conditions – Critical for Representativeness of Results:

- shall be documented and justified (time, temperature, ratio, solvents)
- shall be relevant for conditions during shelf life
- choice of test sample critical (unfilled syringe / syringed filled with extraction medium already during manufacturing)



Before extraction | Condition 1 | Condition 2 | Condition 3

T_1 – Example Liquid Device

Exhaustive Extraction Conditions required:

- several extraction steps might be necessary
- until extracted material is less than 10% of initially extracted amount of material

By this the maximum amount of extractables is reached that can be released from the material under assessment – Toxicological Risk Assessment of those is considered to assume the worst case.

T_1 – Example Liquid Device

Selection of Analytical Methods – Critical for Representativeness of Results

- should be able to detect the substances that are expected as well as possibly unknown substances in toxicologically relevant concentrations!
- should be validated
- should have appropriate sensitivity – LOD/LOQ, AET

  should be considered in the Toxicological Risk Assessment

Questions?

Thank you for your attention!!