Overview: Non-clinical Immunogenicity Assessment of Generic Peptide Products

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Peptide-related Impurities

- For specified impurities common to proposed generic and reference listed drug (RLD)
  - Level in proposed generic ≤ RLD
- For any new impurities in the proposed generic
  - > 0.5% is not acceptable
  - Impurities at 0.1%- 0.5% identified, characterized and justified for not affecting the safety and efficacy, including comparative immunogenicity risk tests

Scientific rationale for the guidance:

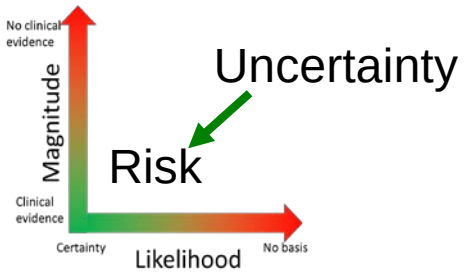
Immunogenicity Risk = Probability X Consequences

- Population ✓
- Treatment ✓
- Product

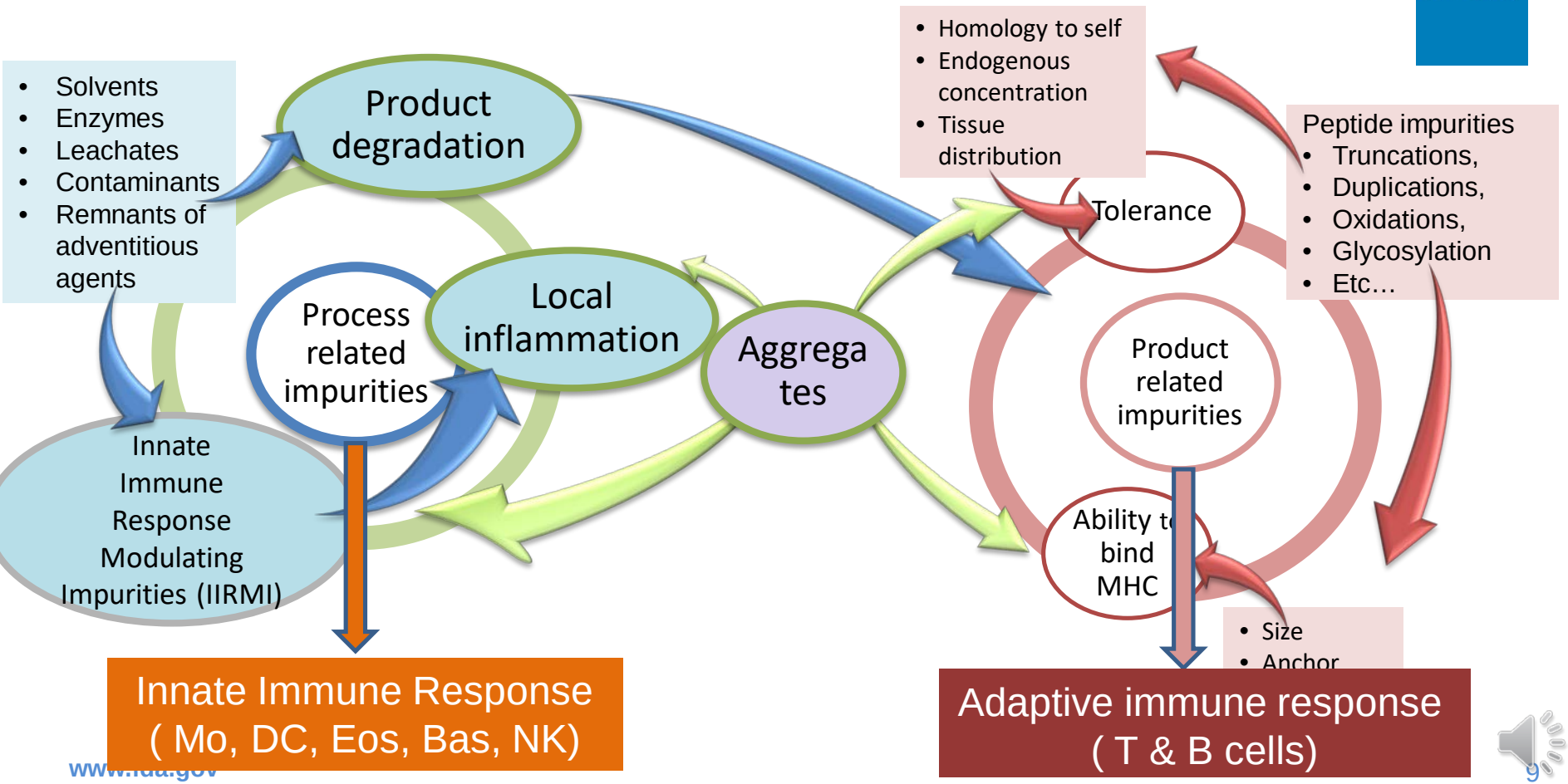
- Safety ✓
- Efficacy ✓

If API is same, then the only residual uncertainty are the impurities

- Product-related impurities
- Process-related impurities
- Aggregates



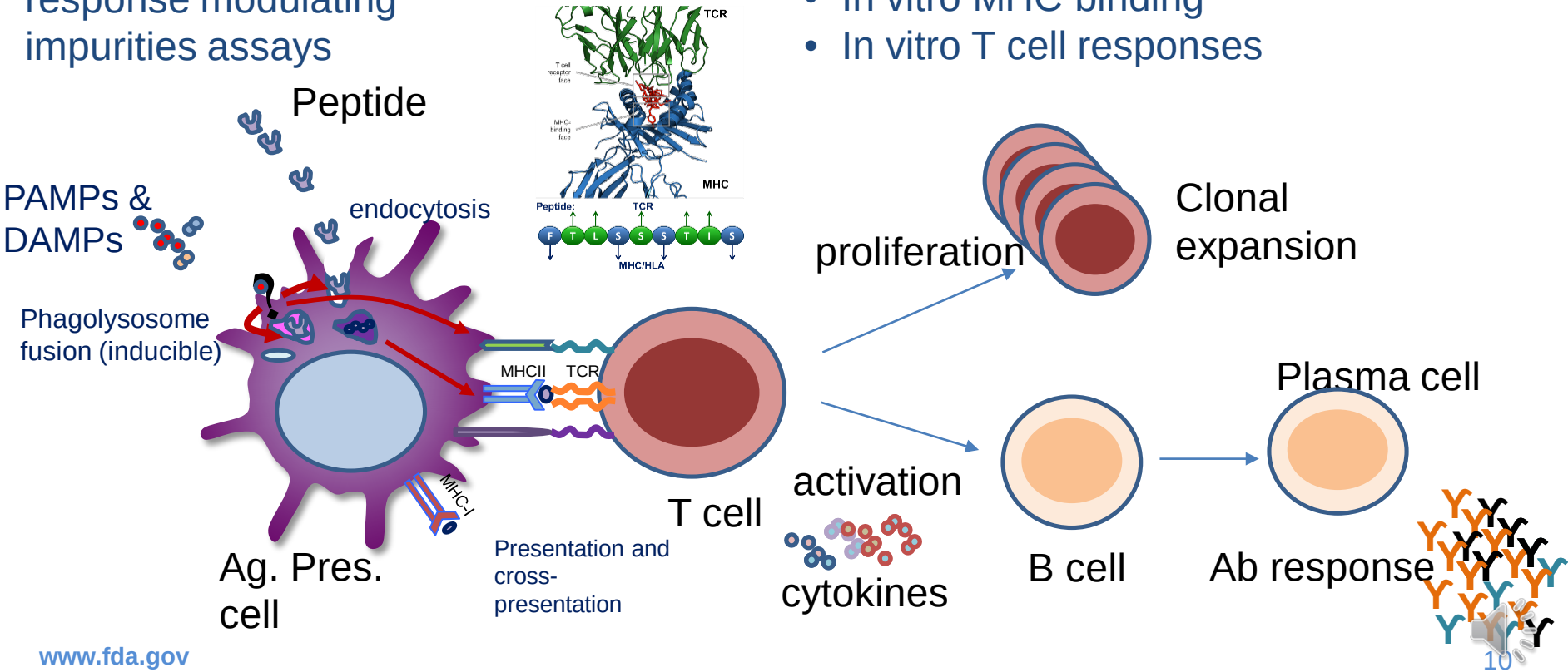
Product and Process Related Impurities:



Immune response: risk assessment tools

- Innate immune response modulating impurities assays

- In silico 1ry sequence
- In vitro MHC binding
- In vitro T cell responses



Criteria: No Increased Risk relative to the RLD

- Assessing the risk of product and process related impurities is not sufficient to determine the immunogenicity risk, but can support, as part of a totality of evidence approach, a risk assessment of “relative” immunogenicity risk as compared to the product that was used in clinical trials.

- However, establishing “no increased risk” requires well-validated assays with demonstrated capability of detecting impurities that impact on immunogenicity risk.

Objective of the Workshop

- Discuss regulatory concerns and considerations regarding the use of non-clinical assays for immunogenicity assessment of generic peptides
- Foster communication regarding technical challenges with validating or performing assays to assess immunogenicity risk and help establish best practices.
- Explore future research directions that the facilitate the performance of sensitive and reproducible assays to assess the immunogenicity risk of impurities in generic peptide products