

# Biocompatibility Update from CDRH

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# Introduction

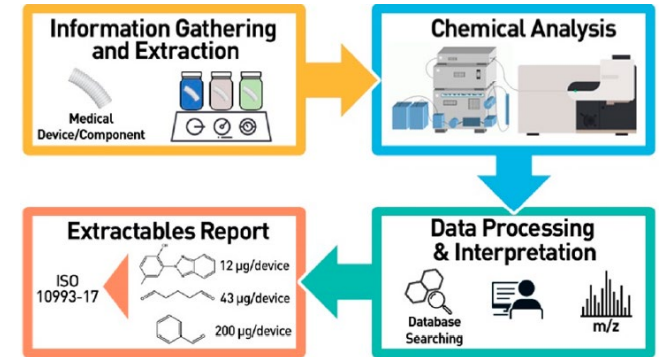
- Review of AFDO RAPS MedCon 2022
  - Chemical characterization and new Guidance(s)
  - CHRIS (as MDDT), safety summaries
  - Formats for premarket sections
- Current Projects and Activities?
  - ASCA
  - In vitro irritation and 10993 Part 23
  - Other Reg Science Research
- What are we going to do next?
  - 2 new workstreams with the AdvaMed biocompatibility members group

# Current Projects (last year)

- Clarification of analytical chemistry thoughts:
  - FDA and AdvaMed biocomp/ chemistry group jointly discussed possible approaches
  - Publication in ACS Biomaterials Science and Engineering
    - (<https://doi.org/10.1021/acsbiomaterials.1c01119>)
  - Will get embodied in technical guidance in due course
  
- Suggested formats for sections
  - Helps reviewers find the most important parts in The Lord of The Rings
  
- ASCA
  - 86 labs accredited to ASCA, 1 in biocompatibility
  - 5 Accreditation bodies

# Status of Current Projects (last year)

- Clarification of chemical characterization thoughts:
  - Draft Guidance document in clearance prior to publication
- Suggested formats for sections
  - Existence embodied in new chemical characterization Guidance
  - Will be available via FDA.GOV so that changes and additions are easier
- Chemical Risk Calculator for Color Additives qualified as MDDT
  - Available at <https://chris-osel.pythonanywhere.com>
  - Next calculator (other additives) entering qualification program



# ASCA

- 97 labs accredited, including 3 in biocompatibility
  - c20 premarket applications to date
  
- Voluntary scheme to become accredited to conduct 9 specific tests:
  - USP <151>
  - Part 4: Complement activation, hemolysis
  - Part 5: MEM elution cytotoxicity
  - Part 10: Closed patch sensitization, guinea pig Maximization sensitization
  - Part 11: Acute systemic toxicity
  - Part 12: Sample preparation
  - Part 23: In vivo dermal irritation, intracutaneous reactivity irritation

# ASCA

- **ASCA Vision:**
  - Reduction of burden for both industry and FDA
  - Possible expansion to include genotox (Ames, in vitro mouse lymphoma, chromosomal aberration) and more hemocompatibility (PTT, platelet and leukocyte count) based on stakeholders' interest
  
- **ASCA Benefit**
  - ASCA reports have not generated any substantive AI requests
  - Sometimes not identified as ASCA reports, compounded by full report being submitted
  - The most recent file with ASCA biocomp: summary test reports were reviewed in 15 minutes with no questions

# Other Premarket Activities

- Part 23 In vitro irritation
  - CDRH has not received sufficient or appropriate data to recognize in vitro irritation
  - CDRH fully intends to recognize in vitro irritation if we can
  - Does it lead us to the same regulatory decision?
  
  - We have received 152 matched pairs of IVIVC data (thank you)
    - Most demonstrate agreement between in vivo and in vitro
    - A minority do not agree and we need to understand the implications
    - Is it material dependent or weak responders?
    - We may need more +ve control information

# Other Premarket Activities

- Part 10 In vitro Sensitization
  - Working with ISO TC 194/ WG 8 to design a study to qualify OECD methods for use with devices
  
- In vitro Thrombogenicity (flowing blood)
  - Initiating a round robin for standardized best practices for dynamic thrombogenicity testing
  
- In vitro Pyrogenicity (monocyte activation)
  - Case by case for endotoxin-related batch release



# What's Next?

- Guidances
  - Draft Analytical Chemistry
  - Final Intact skin in contact with certain polymers (new attachment to FDA Biocompatibility Guidance)
  
- AdvaMed Biocompatibility Group
  - Likely to be 2 new workstreams:
    - Interface between Analytical Chemistry and TRA, with toxicologically relevant DBT
    - Practical approaches to demonstrate biological equivalence



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