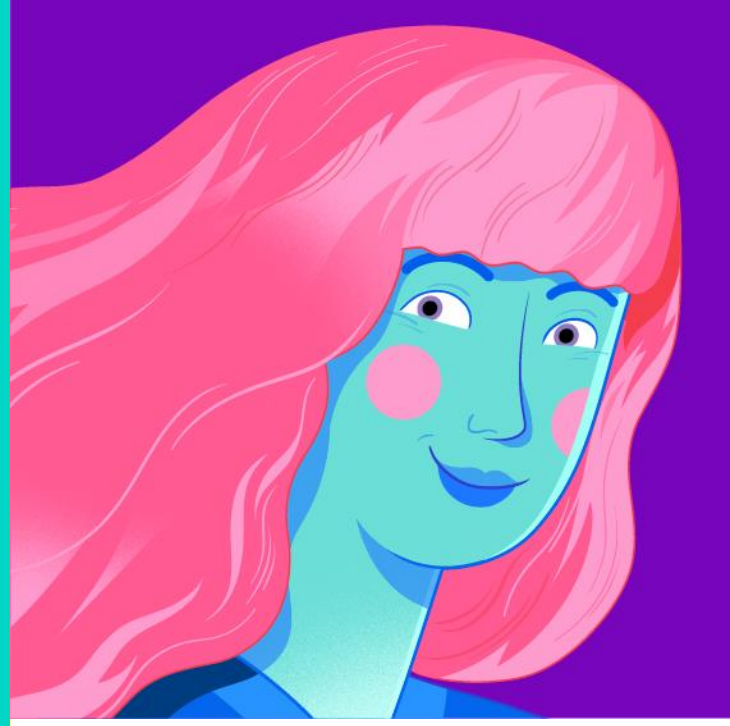
Consumer Goods industry perspective on the benefits of moving towards animal product-free *in vitro* systems



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NC3Rs/Unilever Joint Workshop: Towards the development of animal product free *in vitro* systems

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Consumer Goods industry perspective on the benefits of moving towards animal product-free *in vitro* systems

- There is an increasing acceptance of the role *in vitro* assays can play in assuring consumer safety.
- Many *in vitro* assays contain products derived from animals.
- Removal of all animal-derived products from *in vitro* assays poses a lot of scientific challenges.
- However, these challenges give us opportunity to look at the human relevance of the assays we use as part of making human safety decisions.
- Replacing animal-derived products with chemically-defined products would give the additional advantage of reducing variability between batches/increasing reproducibility of assays.

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Motivations for change: Immune Responses Example

Crit Rev Immunol. 2014;34(5):433-54.

Differences in innate immune response between man and mouse.

Zschaler J[1], Schlorke D[1], Arnhold J[1].

"the direct translation of murine experimental data to human pathological events often fails due to sufficient differences in the organization of the immune system of both species."

Additionally, Foetal Calf Serum can cause unwanted immune modulation effects:

1) Safety issues (such as severe immune reactions)

Tissue Eng Part A. 2010 Jul;16(7):2281-94. doi: 10.1089/ten.TEA.2009.0621.

Differential gene expression in adipose stem cells cultured in allogeneic human serum versus fetal bovine serum.

Lindroos B[1], Aho KL, Kuokkanen H, Räty S, Huhtala H, Lemponen R, Yli-Harja O, Suuronen R, Miettinen S.

2) Non-specific stimulation of T-cells

Biopreserv Biobank. 2011 Sep;9(3):229-236.

Standardized Serum-Free Cryomedia Maintain Peripheral Blood Mononuclear Cell Viability, Recovery, and Antigen-Specific T-Cell Response Compared to Fetal Calf Serum-Based Medium.

Germann A, Schulz JC, Kemp-Kamke B, Zimmermann H, von Briesen H.

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Recommendations from European opinion and advisory committees

1. Scientific Community on Consumer Safety (SCCS) in their document "Basic criteria for the *in vitro* assessment of dermal absorption of cosmetic ingredients" (SCCS/1358/10) recommend using human skin as the "gold standard" mainly due to differences in permeation characteristics.

2. At its 28th meeting on 7-8 May 2008, the Non-Commission members of the ECVAM Scientific Advisory Committee (ESAC) unanimously endorsed the following statement: *"The ESAC members recommend to use non-animal serum substitutes of foetal calf serum (FCS) and other animal derived supplements, whenever possible. For new in vitro culture test methods to be developed the ESAC strongly suggests the use of non animal alternatives to FCS."*

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Opportunity to challenge/reassess the status quo…

One argument often heard for continuing to use animal-products such as FCS is because "that's what has always been done". However, sometimes the components of media can lead to assay interference:

J Extracell Vesicles. 2018 Dec 12;8(1):1552059. doi: 10.1080/20013078.2018.1552059. eCollection 2019.

Technical approaches to reduce interference of Fetal calf serum derived RNA in the analysis of extracellular vesicle RNA from cultured cells.

Driedonks TAP[1], Nijen Twilhaar MK[1], Nolte-'t Hoen ENM[1].

It would be preferable to understand exactly what all the components of the media is when designing an assay, which would also be made easier if the media was chemically defined.

Opportunity to go back to the drawing board and ask the question – what do I actually need in my assay media/buffer etc?

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Remaining challenges & opportunities

Good progress is already being made in the areas of media composition and antibody generation, but important gaps & challenges remain for us to completely transition all our assays away from animal-derived products:

- **Adding metabolism to assays (e.g. S9 alternatives)**
- **Animal-free scaffolds**
- **Encouraging uptake by making the alternatives more widely available & promoting the benefits of these products e.g. some serum-free alternatives have been available for years but uptake has been slow:**

Proc Natl Acad Sci U S A. 1986 Jan; 83(1): 9–13.
doi: 10.1073/pnas.83.1.9
PMCID: PMC322780
PMID: 3079905

Development of a chemically defined serum- and protein-free medium for growth of human peripheral lymphocytes.

W Shive, F Pinkerton, J Humphreys, M M Johnson, W G Hamilton, and K S Matthews

Conclusions

- **Benefits of moving towards animal product-free *in vitro* systems include increased human relevance & consistency of assay components leading to reduced assay interference issues and an increase in assay reproducibility.**

- **Challenges & opportunities remain both in the development of alternatives & subsequent uptake.**

- **Looking forward to hearing your thoughts on this exciting and rapidly expanding area of science!**

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Thank you!

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