WC10でのリードアクロス関連発表の報告

株式会社　インシリコデータ
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WEDNESDAY, AUGUST 23, 2017

ROOM	08:00-08:30	08:30-09:15	09:15-09:30	09:30-10:00	10:00-12:00	12:00-13:15	13:15-14:45	14:45-15:15	15:15-17:00	17:15-18:00	19:30-22:00
6E	Moring Coffee	PLENARY LECTURE Hiroaki Kitano	AWARDS CEREMONY	Break		Lunch Break		Break		PLENARY LECTURE Russell S. Thomas	Gala Reception
606					SESSION II-5 Read Across		SESSION IV-3 Educating and Training Scientists to be Future Leaders in Sustainability		SESSION VI-2 Knowledge Sharing in Promoting 3Rs Advances		
608					SESSION VII-4 21st Century Cell Culture Practices		SESSION VIII-1 Evolution of Research Animal Welfare		SESSION III-10 Models Used for Ecology and Ecotoxicology		
609					SESSION II-6 Integrating In Vitro to Predict Organ Tox				SESSION V-3 Best Practices for Modeling Data		
611-612							SESSION I-3 Ethical Selection of Species – Round Table		SESSION VIII-6 Training Animals for Better Science and as Partners in Scientific Process		
613-614					SESSION VIII-2 Advances in Technology to Enhance Animal		SESSION II-4 Eye Hazard Potential Examples		SESSION V-4 Resources and Tools for State of the Art Systems Modeling		

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09:15–09:30 Room 6E

Awards

ALTEX Award Ceremony

10:00–12:00 Room 606

Session II-5: Read Across

Co-Chairs: **Grace Patlewicz**, USEPA, RTP, NC, USA

Masamitsu Honma, National Institute of Health Sciences, Tokyo, Japan

II-5-432 Grace Patlewicz: Navigating Through the Minefield of Read-Across: From Research to Practical Tools

II-5-645 Sunil Kulkarni: Read-Across: Lessons Learned & Success Stories from Canada's Chemicals Management Plan

II-5-561 Takashi Yamada: Our Recent Experiences for Development of Read-across Approach for Chemical Safety Assessment

II-5-671 Francis Kruszewski: Benefits of Using Read Across and in Silico Techniques to Fill Non-SIDS Data Gaps for High Production Volume Chemical Categories

II-5-126 George Helman: Case Study of Read-across Predictions Using a Generalized Read-Across (GenRA) Approach

II-5-632 Q. Jay Zhao: Application of Read-Across in Quantitative Chemical Risk Assessment in a Regulatory Setting

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Stanton Kruszewski_Quantifying Benefits Using Read Across_RTP 81_250-259_2016.pdf - Adobe Acrobat Reader DC
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Quantifying the benefits of using read-across and *in silico* techniques to fulfill hazard data requirements for chemical categories

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ABSTRACT

Substantial benefits are realized through the use of read-across and *in silico* techniques to fill data gaps for structurally similar substances. Considerable experience in applying these techniques was gained under two voluntary high production volume (HPV) chemical programs – the International Council of Chemical Associations' (ICCA) Cooperative Chemicals Assessment Programme (with the cooperation of the Organization of Economic Cooperation and Development) and the U.S. Environmental Protection Agency's HPV Challenge Program. These programs led to the compilation and public availability of baseline sets of health and environmental effects data for thousands of chemicals. The American Cleaning Institute's (ACI) contribution to these national and global efforts included the compilation of these datasets for 261 substances. Chemicals that have structural similarities are likely to have similar environmental fate, physical-chemical and toxicological properties, which was confirmed by examining available data from across the range of substances within categories of structurally similar HPV chemicals. These similarities allowed the utilization of read-across, trend analysis techniques and qualitative

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Benefits of reduced physico-chemical testing	3,720,208	N/A
Total	54,149,579–67,527,701	115,502–149,542

avoidance of toxicity testing overall resulted in between 50,429,300 and 63,807,500 USD of savings. If performed today, the total testing cost across all endpoints and all 261 substances in nine HPV categories would be between 54,149,580 and 67,527,700 USD (Table 8).

4. Discussion and conclusion

In the ICCA and EPA programs for high production volume chemicals, many lessons were learned in constructing categories that build scientific confidence in the use of read-across and *in silico* methods to fill data gaps. While read-across, trend analysis and (Q)SAR methods can be used to address information requirements under various regulatory and voluntary programs, the acceptance of alternative approaches to testing hinge on the validity of the category. The nine categories of our analysis were assembled following OECD guidelines and were accepted by OECD member country regulatory experts (Table 1), and/or by the U.S. EPA and other expert stakeholders in the EPA HPV program. Additionally, the hydrotropes and amine oxides categories were included in the compendium of case studies that helped shape REACH guidance on chemical category assembly and read-across (Worth and Patlewicz, 2007). Further acceptance of the category approach was realized outside of the regulatory and voluntary programs. Ten papers grounded in the hazard and risk assessments of four of the categories were published in peer-reviewed publications, namely alkyl sulfates, alkane sulfonates and olefins, amine oxides, hydrotropes, and long chain alcohols (see Sanderson et al., 2006; Stanton et al., 2009; Belanger et al., 2009; Fisk et al., 2009; Sanderson et al., 2009a, 2009b; Schäfers et al., 2009; Veenstra et al., 2009; Könnecker et al., 2011; Wibbertmann et al., 2011), adding another layer of scientific review to validate the legitimacy and robustness of the category approach for these chemical groups.

As the categories were agreed upon by the regulatory experts, so were the hazard assessments. For those substances which have been assessed within the OECD Programme, the summary of the conclusions on the hazards have been reviewed by experts in member countries (Table 1), industry and environmental NGOs and are endorsed by participating OECD member countries. The chemical category assessments submitted under the U.S. EPA Program also underwent expert regulatory and stakeholder review. In some cases, the expert reviews praised the use of read-across to fill data gaps in lieu of animal experimentation (Manuppello, 2008).

While there are studies which forecast animal use and cost estimates for the purposes of fulfilling data requirements under different legislative regimes such as REACH (see for example Rovida and Hartung, 2009; Höfer et al., 2004; van der Jagt et al., 2004; Pedersen et al., 2003; RPA and Statistics Sweden, 2002; IEH Report, 2001), this is the first analysis of actual avoided test animal use and cost savings. The analysis herein is specific to the SIDS hazard endpoints gathered for the purposes of the HPV voluntary programs under U.S. EPA and ICCA for 261 chemicals. The analysis assumes universal testing using OECD tests for filling data gaps. While the use of read-across and *in silico* techniques to fill data gaps for the 18 hazard endpoints across the 261 substances of this assessment are considered by the U.S. EPA and the OECD country experts participating in the ICCA program to be scientifically justified, it is acknowledged that regulatory jurisdictions can vary in their degree of acceptance of or familiarity with the use of these alternative techniques to fulfill statutory requirements. Consequently, the degree to which these approaches are applicable in specific jurisdictions will be understood through the consultation of respective statutory language and regulatory guidance documents.

The use of read-across and *in silico* methods for filling gaps where hazard data are lacking for specific chemicals within categories of chemicals has many benefits. First and foremost, ACI consortia demonstrated a firm adherence to the Three Rs (Replacement, Reduction, Refinement) as guiding principles for the more ethical use of animals in testing (Russell and Burch, 1959). By eliminating the need for animal testing through the use of read-across and *in silico* methods where scientifically justified, the use of between 115,500 and 149,500 animals in toxicity tests, specifically between 108,500 and 142,500 rodents and 7000 fish, was avoided. Among the SIDS endpoints that require vertebrate animals, testing was completely avoided by using read-across and *in silico* methods.

The substantial reductions in testing costs was another significant benefit achieved in the ACI program through the application of these techniques. With the ability to compile publicly-available and privately-held data on chemicals, group chemicals into valid categories based on expert judgement and guidance, and use read-across, trend analyses and (Q)SARs methods to fill data gaps, there was between 54,000,000 and 67,500,000 USD saved to complete hazard-level screening assessments for 261 chemicals.

Acknowledgements

A substantial amount of the data used as the basis for the assessments cited in this manuscript were provided by the 62 companies engaged in the SDA/ACI consortia. We would like to thank the members of the consortia for their commitment to animal welfare through the use of alternative methods.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.yrtph.2016.09.004.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.yrtph.2016.09.004

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Benefits of Using Read-Across and *In Silico* Techniques to Fill Non-SIDS Data Gaps for High Production Chemical Categories

Francis Kruszewski and Kathleen Stanton

American Cleaning Institute

August 23, 2017

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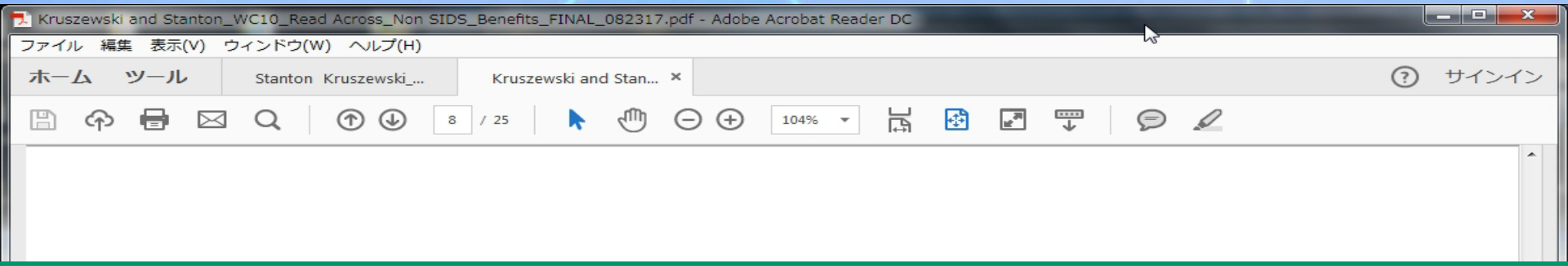

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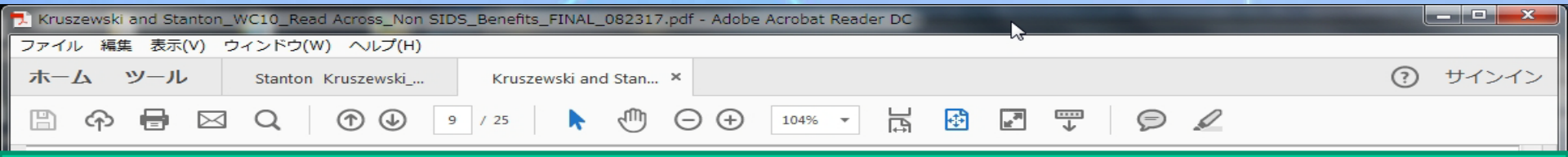

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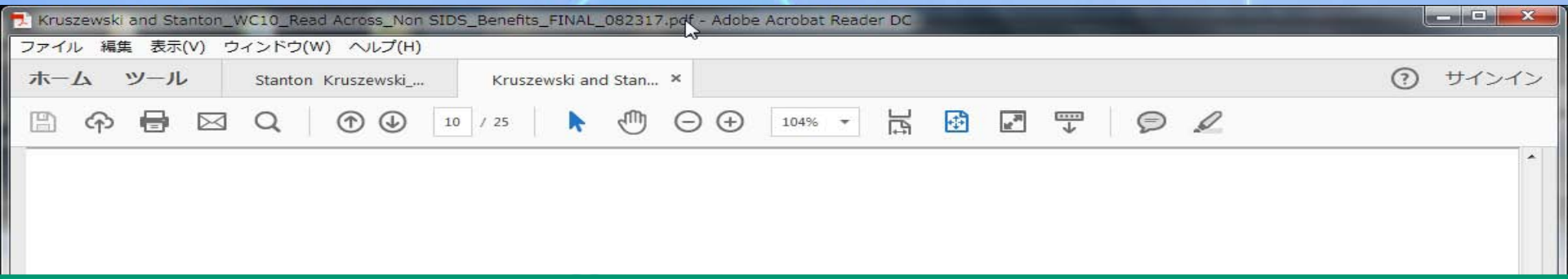

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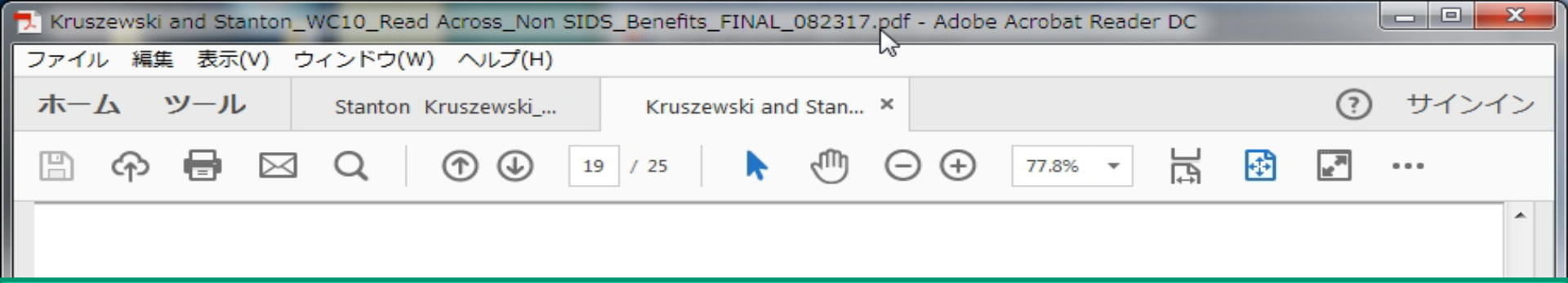

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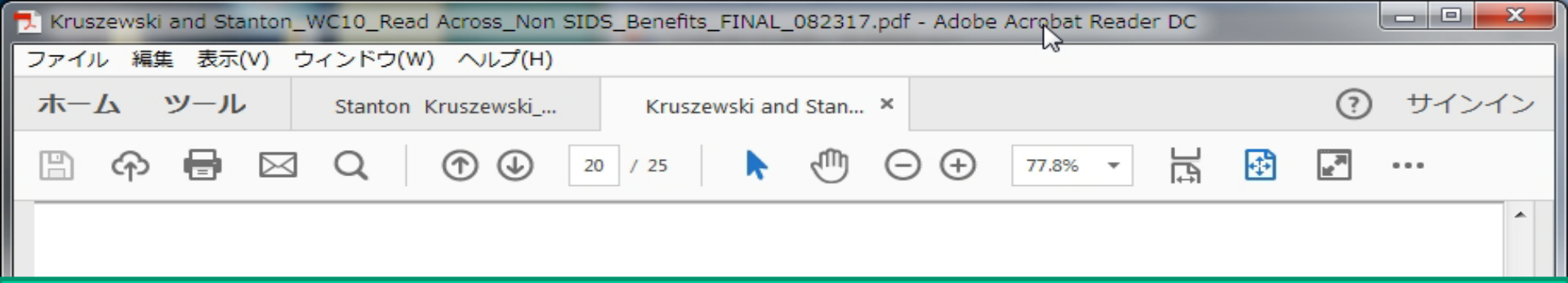

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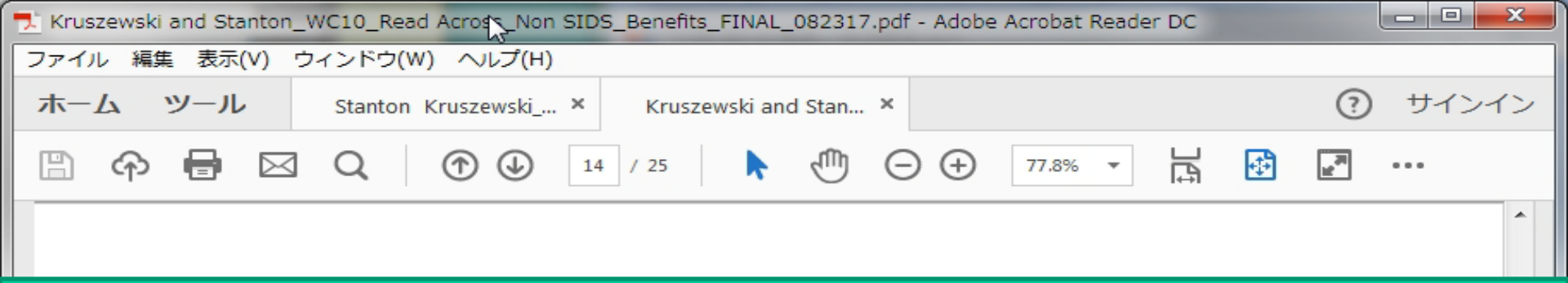

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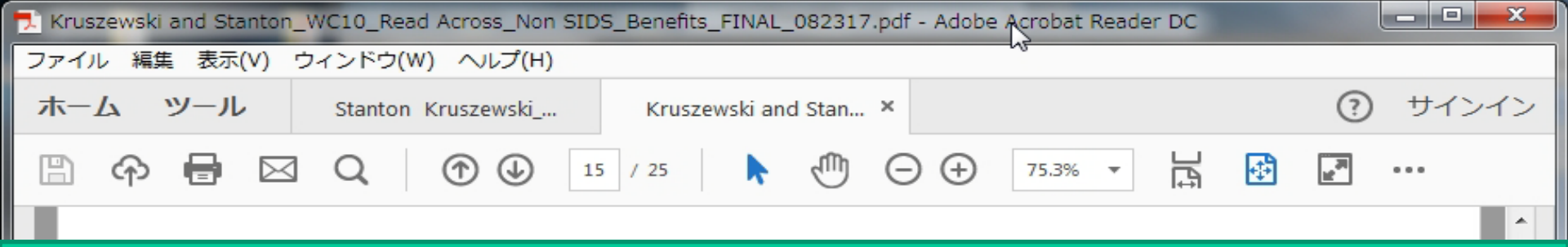

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Conclusions

- HPV Submissions by ACI to OECD and EPA provide publically available data on chemical testing
- Available data represent both SIDS and Non-SIDS endpoints
- Available data can be useful for meeting REACH requirements
- Use of Read Across and *in silico* techniques have provided benefits in reducing testing costs and avoiding animal testing
- ACI HPV submissions can be accessed on OECD or ACI websites

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Thank you for your attention

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