Drivers for Adoption

Ensuring Acceptance and Compliance by the Research Community

The following Consensus Building Paper presents key topics described in the following sources: comments from pre-workshop online discussions made on protocols.io; feedback from the Workshop Steering Committee; and relevant publications. All content not referenced is derived from online discussions. Source material as of August 30, 2016.

The purpose of this paper is to provide a starting off point for the dialogues and consensus-building process at the *Antibody Validation: Standards, Policies, and Practices* Workshop. The conclusions and preliminary recommendations are not final but are meant to serve as a basis for further discussion.

Irreproducibility of scientific research is at the forefront of problems limiting scientific progress and translating basic and applied research (Begley & Ellis, 2012; Freedman et al, 2015a; Freedman & Inglese, 2014; Hartshorne & Schachner, 2012). The ability to replicate scientific research is tied to the assumption that biological reagents function as intended and in a reproducible manner, and yet a general lack of defined standards and best practices in life sciences research exists to ensure this (Freedman & Inglese, 2014). Incomplete or improper antibody validation has been identified as a major source of irreproducibility (Baker, 2015; Begley & Ellis, 2012; Bradbury & Pluckthun, 2015; Marx, 2013; Weller, 2016). The concepts, perspectives, and preliminary recommendations described herein are derived from the pre-workshop online dialogues and published literature. The preliminary recommendations are intended to promote thoughtful consideration of approaches for promoting acceptance and compliance of antibody validation standards within the research community. This paper will serve as a basis for building consensus at the Antibody Validation: Standards, Policies, and Practices Workshop.

Barriers to Successful Adoption and Implementation | Despite the need for antibody validation standards, careful consideration of the barriers to the adoption of widely-accepted and used standards is crucial. Potential barriers identified in the online dialogues include monetary costs, time requirements, the complexity of the existing market, and reliance on commercial producers to implement change. Engaging key stakeholders during the process of building consensus on rigorous and practical standards that acknowledge these barriers will drive its adoption.

Role of Funders | Funders play a critical role in promoting communication of validation standards, developing and maintaining community resources (e.g., curricula for graduate training and education, proficiency testing programs, and databases), and incentivizing the practice of antibody validation within the research community. Figure 1 highlights several ways that funders can influence adoption of validation standards and support antibody validation proficiency (Freedman et al, 2015a; Freedman et al, 2015b).

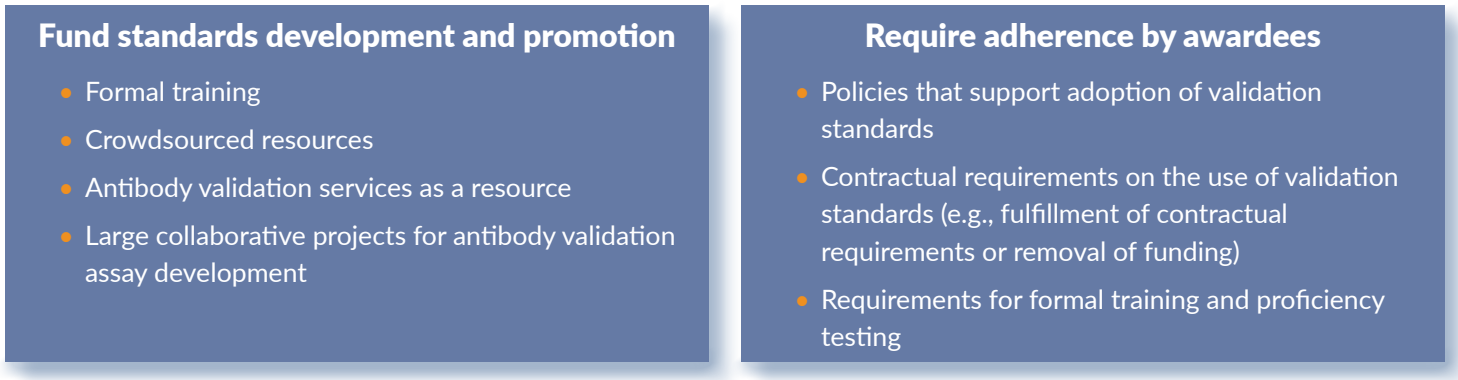

Figure 1 **Potential roles of funders in support of robust and rigorous standards for antibody validation:** Summarizes mechanisms for promoting the implementation of antibody validation standards to encourage rigorous, reproducible research

In January 2016, the National Institutes of Health instituted new requirements for demonstrating reagent-validation in grant applications as part of its Rigor and Reproducibility Initiative. All grant submissions now must contain information on the authentication of key biological and chemical resources. Although its impact has yet to be determined, this requirement exemplifies the potential role of funders in promoting awareness and enforcing adoption of validation practices.

Published originally in April 2011 and revised July 2015, the Research Councils UK requires a data-availability statement be included in all research grant applications, and it is possible that other public and private funders could include this as a requirement for funding.

Supporting Validation Standards through Journals | Failure to thoroughly report and track antibody use in research publications contributes to difficulties in replicating earlier work (Helsby et al, 2013). Figure 2 summarizes the information on antibody validation requested by 19 different publishers and organizations. While some journals have specific guidelines for communicating information about the antibodies used in research and support validation, a significant amount of variability exists in what is required or simply requested. As part of editorial review, journals are uniquely positioned to require that antibody validation data be made available. The potential role of journals in promoting existing initiatives and associated challenges as identified in online dialogues are shown in Figure 3 and Text Box 4. A quick review of several life-science journals reveals the following requirements for authors, specifically relating to research antibodies:

- Established guidelines for authors ensure transparency and information-sharing. These guidelines might include detailed information on the use of antibodies across applications and validation strategies that demonstrate the suitability of key biological reagents (Nosek et al, 2015) (Text Box 4A).
- New initiatives by publishers enable reporting of detailed methods and information on resources and reagents supporting reproducibility (Text Box 4B and 4C).
- A consistent and unique identifier for antibodies used across publications and journals would enable effective tracking of reagents, promoting reproducibility (Bandrowski et al, 2015). New publishing practices are supporting the use of unique identifiers and allowing direct links to existing antibody databases that curate validation information (Text Box 4D).
- Badging systems could incentivize authors to perform robust validation and transparent data-sharing without burdening editorial staff. An outside entity could enable this (Kidwell et al, 2016) (Text Box 4E).

TOP Guidelines	The Center for Open has developed "Transparency and Openness Promotion Guidelines" for journals, such as Science and the PLOS family. These include eight standards with stringency levels that journals should enforce.
Structured Transparent Accessible Reporting (STAR) Methods	Cell Press journals have implemented a new structured methods section for reporting experimental design and methodological details. This includes a table with information on key resources and reagents.
Data-sharing Statement	The Nature Publishing Group (NPG) now also requires that authors complete a data-sharing statement detailing if and where they are sharing their data, and where.
Publishing Checklists	NPG now requires that authors validate antibodies in each specific experiment and species as part of a publishing checklist (Helsby et al, 2013). *BioTechniques* guidelines require that batch and lot numbers be included in author submission.
RRID	Resource Identifiers (RRIDs) as part of the resource identification initiative allows researchers to cite reagents, including antibodies, consistently across the literature by assigning curated identifiers.
Badging	The Center for Open Science has developed a badging system to highlight best practices for open data, and materials and registration of studies for display in publications.

Journal / Organization	Unique Materials Availability / Identification	RRID Participation	Ab Validation Requirements	Validation Requirement Strictness*
1	Yes	Required	Yes	In-depth
2	Yes	Required	Yes	In-depth
3	Yes	No	Yes	In-depth
4	Yes	No	Yes	In-depth
5	Yes	Encouraged	Yes	Intermediate
6	Yes	No	Yes	Intermediate
7	Yes	No	Yes	Intermediate
8	Yes	No	Yes	Intermediate
9	Yes	Encouraged	No	Minor
10	Yes	Encouraged	No	Minor
11	Yes	Encouraged	No	Minor
12	Yes	Encouraged	No	Minor
13	Yes	Encouraged	No	Minor
14	Yes	No	No	Minor
15	Yes	No	No	Minor
16	Yes	No	No	Minor
17	Yes	No	No	Minor
18	Yes	No	No	Minor
19		No	Yes	Intermediate

Figure 2 **Existing transparency, reagent sharing, and validation practices related to antibody-based research from publishers and other organizations**

Details information on relevant publication requirements from 19 publishers and other organizations. A relative determination of antibody validation rigor is shown by identifying each journal as in-depth, intermediate, or minor.

Challenges for rigorous reporting of antibody validation data by journals

- Reporting and information sharing requirements about antibody validation may be difficult given limited funding and already high editorial volumes;
- Editorial staff may not be trained for antibody validation assessment. In addition, not all journals have professional editors, which might limit their ability to consistently assess antibody validation results;
- Existing initiatives, such as badging, which could be established by funders, journals, or other independent organizations, must have their requirements clearly defined and may not be practical due to issues with implementation.

Figure 3 Describes potential challenges for journals in reinforcing antibody validation standards and using certain initiatives (e.g., badging), as conveyed through the online discussions.

Training and Proficiency Testing | The broad adoption of antibody validation standards by the research community is closely tied to education and training. A recent survey by GBSI highlighted the critical need for better training (Freedman et al, 2016). The percentage of junior researchers who reported validating antibodies (43%) was substantially lower than senior scientists (70%). Strikingly, Figure 4 reflects that a third of junior researchers did not report validating antibodies at all. This finding supports providing less-experienced researchers with formal training on the need for validation of antibodies used in research and the science behind antibody validation. Additionally, the results indicate that the importance of antibody validation may not be communicated or emphasized effectively by senior researchers, providing another reason for training. Specific solutions focused on training and proficiency include; (Freedman et al, 2016; Freedman et al, 2015b):

- Improvements of formal graduate-level training programs on underlying principles of antibody-based research and antibody validation; and
- Training and proficiency programs for senior researchers that communicate and reinforce best practices for antibody validation.

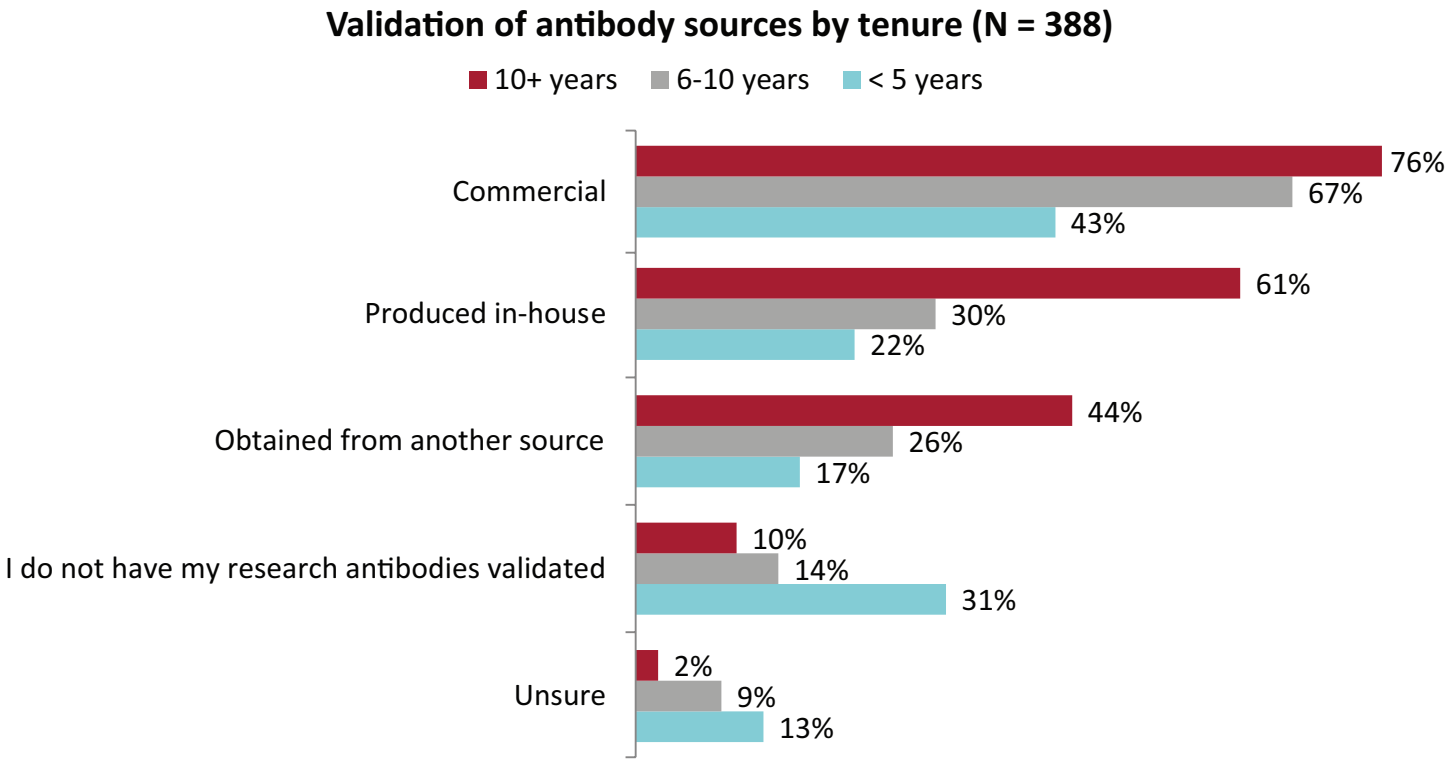

Figure 4 Validation of antibody sources by tenure

Recommendations for Discussion | Preliminary recommendations on the roles of funders, journals, educators, and researchers in promoting and establishing scientific standards for antibody validation based on the online dialogues and literature are presented below.

- Funders play a significant role in promoting implementation of, proficiency in, and communication of antibody validation through various means, including requirements in grant applications, support for graduate-level training and proficiency testing programs, and encouragement of senior-level refresher courses. These initiatives should enforce rigorous science and consistent application of validation standards.
- Journals should support requirements for transparent methods, information-sharing, and best practices for antibody validation. If feasible, they should support the use of reagent continuity efforts (e.g., RRIDs).
- Journals and researchers should consider the use of badging systems to promote and incentivize the sharing of validation data.
- Researchers should perform antibody validation, comply with guidelines, and share validation data with the broader life-science community.

Concluding Remarks | The successful adoption and implementation of antibody validation standards in support of robust and reproducible research is multifactorial and requires a delicate balance between antibody validation and key barriers to adoption. Funders, educators, journals editors, and researchers all play a role to lend cohesive support of methods for adoption, implementation, and enforcement.

References

Baker M (2015) Reproducibility crisis: Blame it on the antibodies. *Nature* 521: 274-276

Bandrowski A et al (2015) The Resource Identification Initiative: A cultural shift in publishing. *F1000Research* 4: 134

Begley CG, Ellis LM (2012) Drug development: Raise standards for preclinical cancer research. *Nature* 483: 531-533

Bradbury A, Pluckthun A (2015) Reproducibility: Standardize antibodies used in research. *Nature* 518: 27-29

Freedman LP et al (2015a) The Economics of Reproducibility in Preclinical Research. *PLoS biology* 13: e1002165

Freedman LP et al (2016) [Letter to the Editor] The need for improved education and training in research antibody usage and validation practices. *BioTechniques* 61: 16-18

Freedman LP et al (2015b) Reproducibility: changing the policies and culture of cell line authentication. *Nature methods* 12: 493-497

Freedman LP, Inglese J (2014) The increasing urgency for standards in basic biologic research. *Cancer research* 74: 4024-4029

Hartshorne JK, Schachner A (2012) Tracking replicability as a method of post-publication open evaluation. *Frontiers in computational neuroscience* 6: 8

Helsby MA et al (2013) Reporting research antibody use: how to increase experimental reproducibility. *F1000Research* 2: 153

Kidwell MC et al (2016) Badges to Acknowledge Open Practices: A Simple, Low-Cost, Effective Method for Increasing Transparency. *PLoS biology* 14: e1002456

Marx V (2013) Finding the right antibody for the job. *Nat Meth* 10: 703-707

Nosek BA et al (2015) SCIENTIFIC STANDARDS. Promoting an open research culture. *Science (New York, NY)* 348: 1422-1425

Weller MG (2016) Quality Issues of Research Antibodies. *Analytical chemistry insights* 11: 21-27

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