

NCATS

Improving Health Through Smarter Science

Assay Guidance Manual

The Assay Guidance Manual (AGM) is a free, best-practices online resource for the successful development of robust, early-stage drug discovery assays. These assays are tests that enable researchers to examine thousands of compounds using automated screening systems in an effort to develop chemical probes and drug candidates.

The National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH), manages the AGM in collaboration with Eli Lilly and Company. The AGM provides researchers worldwide with step-by-step guidance to facilitate the discovery of pharmacological tools and drugs.

AGM goals include:

- Sharing best practices in quantitative biology,
- Sharing best practices in the development of robust assay methods throughout the drug discovery community, and
- Enhancing academic-industrial collaborations in translational biology and medicine.

NCATS aims to overcome obstacles in translation — the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public — by developing novel approaches, technologies, resources and models; demonstrating their usefulness; and disseminating this information to the community.

Overview

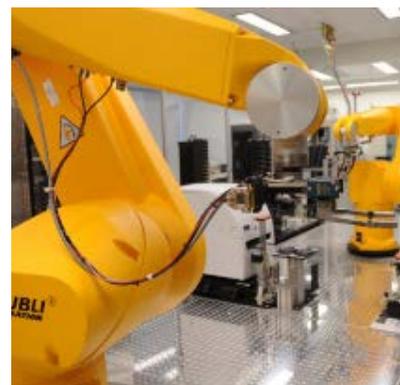
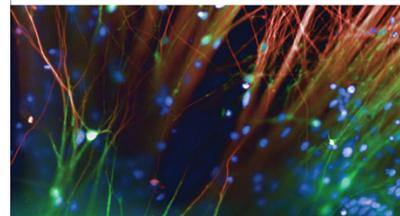
The AGM was originally developed by Eli Lilly and Company in the 1990s to provide guidance, based on “tribal knowledge” from drug developers, for planning and implementing projects involving high-throughput screening, lead optimization and early phases of regulated drug development. Tribal knowledge is any unwritten, well-tested information that is not commonly known by others within an institution. The well-tested methods outlined in the manual accommodate minor changes to assay protocols to ensure robustness. Appropriate statistical analysis methods and concepts are also discussed.

The manual has evolved over time with contributions by more than 100 scientists from industry, academia and government agencies worldwide. NIH publishes the [online manual](#) on the National Library of Medicine’s National Center for Biotechnology Information website, which provides access to a large audience, enables PubMed citations for contributing authors and supports quarterly updates to maintain high quality.

Investigators can use the AGM to design biologically and pharmacologically relevant assays compatible with high-throughput screening and structure–activity relationship (SAR) measurements of new and known molecular compounds. What previously served as proprietary information now is a valuable resource for the research community for robust, reproducible assay results.

ncats.nih.gov/agm

THE ASSAY GUIDANCE MANUAL



U.S. Department of Health
and Human Services

National Institutes of Health

NIH...Turning Discovery Into Health

NIH National Center
for Advancing
Translational Sciences

AGM Development and Maintenance

AGM chapters are written by authors who are experts in their fields and edited by representatives from industry, academia and government. This eBook is a comprehensive, crucial resource for investigators optimizing assays to evaluate collections of molecules with the overall goal of developing probes that modulate the activity of biological targets, pathways or cellular phenotypes. Such probes might be candidates for further optimization and investigation in drug discovery and development.

The AGM addresses:

- Descriptions of assay formats that are compatible with high-throughput screening and SAR measurements of new and known molecular entities.
- Selection and development of optimal assay reagents.
- Optimizations and troubleshooting for assay protocols with respect to sensitivity, dynamic range, signal intensity and stability.
- Adaptations of assays for automation and scaling to microtiter plate formats.
- Instrumentation.
- Mitigation of assay artifacts and interferences.
- Statistical validation of assay performance parameters.
- Secondary assays for chemical probe validation and SAR refinement.
- Data standards for reporting the results of screening and SAR assays.
- *In vivo* assay development and validation.
- Assay development and validation for siRNA-based high-throughput screens.

As new chapters are added to the manual, the goal is to cover all aspects of pre-clinical development. The editors seek new chapters on assays involving biophysical methods, phenotypic screening, stem cells, 3-D cell cultures, pharmacokinetics, pharmacodynamics and toxicology.

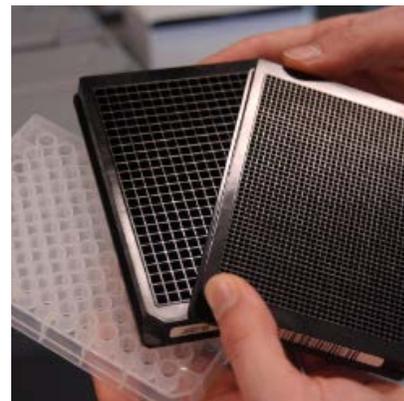
Chapters provided by contributing authors are peer-reviewed, receive PubMed ID numbers and are considered scientific publications. NCATS encourages interested individuals to contact the AGM editors at NCATS_AGM_Editors@mail.nih.gov to discuss opportunities for new contributions.

AGM Training

To address growing interest in high-throughput screening and lead discovery, NCATS offers several **AGM training workshops** throughout the year. Each workshop is designed to share best practices and advice on robust assay design, development and implementation for researchers involved in the drug discovery process.

Instructors, including AGM editors, have 20-30 years of experience in the field of drug discovery and pre-clinical development. Workshops feature valuable training for drug discovery scientists who are planning or beginning to develop test methods for high- or low-throughput screening that are amenable to automation using appropriate statistical and operational concepts. The workshops also are useful for early-career researchers and experienced investigators who want to learn about the latest assay concepts for high-throughput screening and lead optimization.

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For More Information

About the AGM

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AGM Training

ncats.nih.gov/agm-training

View the Manual

ncbi.nlm.nih.gov/books/NBK53196

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