Biomarkers in New Drug Development for Psychiatric Conditions

Pamela Horn, MD
Division of Psychiatry, Office of New Drugs, US FDA
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Disclaimers

- Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position

- I do not have any financial disclosures regarding FDA-regulated products

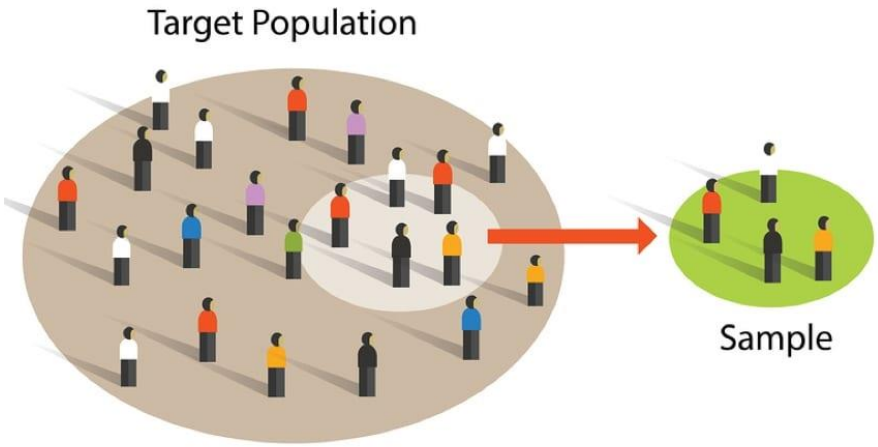
Office of New Drugs

- Responsible for regulatory approval of new drugs in the US
- Resides in the Center for Drug Evaluation and Research (CDER) at FDA
- "The benefits exceed the risks under the conditions stated in the labeling."
  - Safety acceptable for the proposed indication in light of the benefit
- Substantial evidence of effectiveness is required for FDA approval (Section 505(d) of the FD&C Act)

> "Evidence consisting of adequate and well-controlled investigations…, on the basis of which it could …be concluded…that the drug will have the effect it ..is represented to have under the conditions of use prescribed, recommended, or suggested in…labeling"

Target population

- Study populations should reflect the target population
- Need to know if all with condition are suitable for treatment
- Prescriber must be able to determine whether an individual patient is suitable for treatment with the drug



Division of Psychiatry (DP)

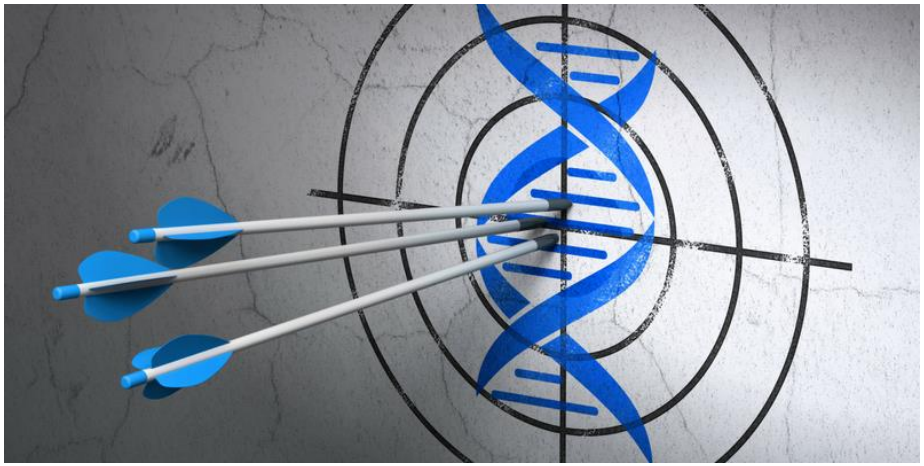
Reviews drugs for treatment of*

- Mood disorders
- Anxiety & OC disorders
- Psychotic disorders
- Trauma-related Disorders
- Attention deficit hyperactivity disorder
- Tourette syndrome
- Tardive dyskinesia
- Behavioral sx of dementia
- Behavioral sx of genetic syndromes
- Autism spectrum disorders
- Sleep disorders

*DP does NOT review drugs for the treatment of substance use disorders: reviewed by Division of Anesthesiology, Addiction Medicine and Pain Medicine(DAAP)

Precision in Psychiatric Drug Trials

- Study population selection could be improved by new approaches to increasing diagnostic accuracy
- Treatment effect measurement could be improved by identifying new predictive and prognostic factors and addressing them in randomization and statistical analysis

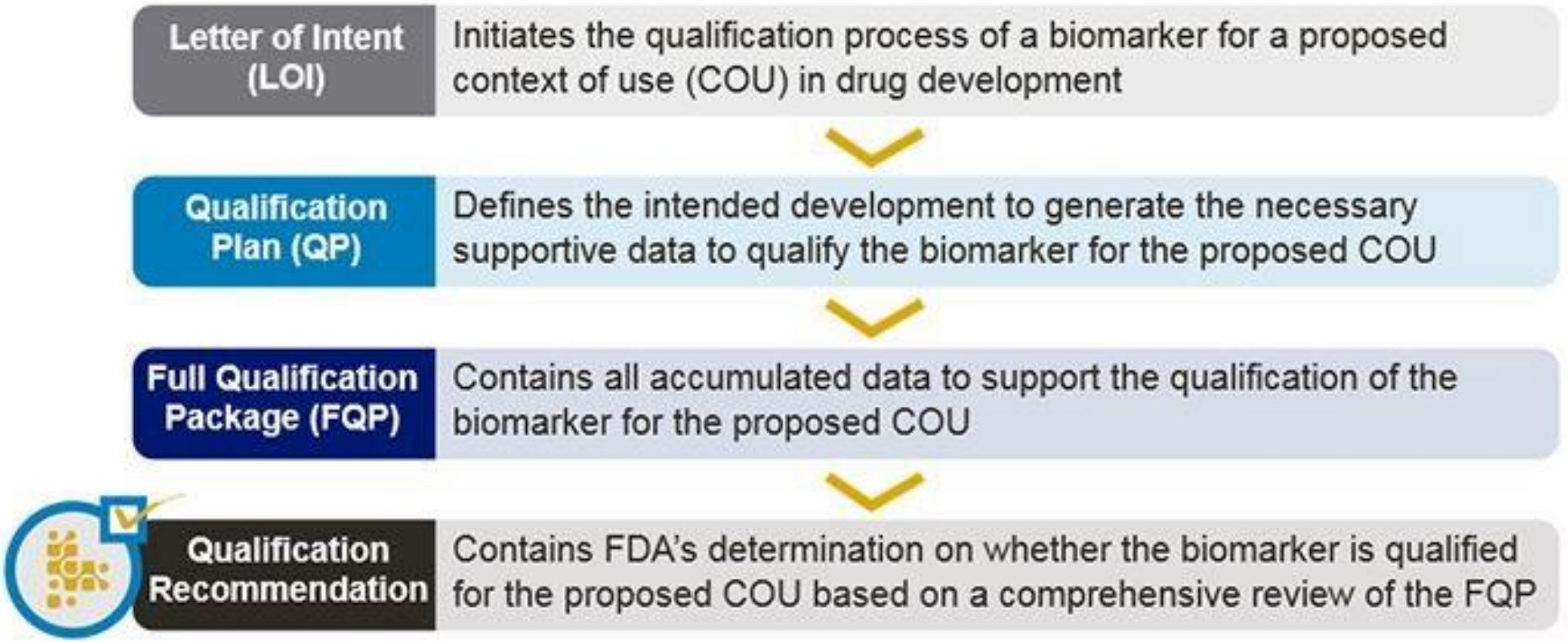


Potential Role of Biomarkers in AWC Drug Studies

- Susceptibility/ risk: Use as part of entry criteria to identify risk of developing disease
- Diagnostic: Use as part of entry criteria to confirm diagnosis (genetic syndromes with neuropsychiatric symptom targets)
- Prognostic: Identifies likelihood of clinical outcome but does not interact with treatment; select and enrich study population to improve precision in measurement of treatment effect or use as covariate in analysis (repeat length or copy number correlates with severity)
- Predictive: Predicts treatment effect; select and enrich study population or separate analyses by biomarker-based subgroup
- Pharmacodynamic/response: Biological response to a drug, may have potential to be used as a surrogate endpoint
- Monitoring: Measured repeatedly for assessing status of response (urine or blood levels of drug of abuse in SUD trial)
- Safety: measurement of drug toxicity (neutrophil count)

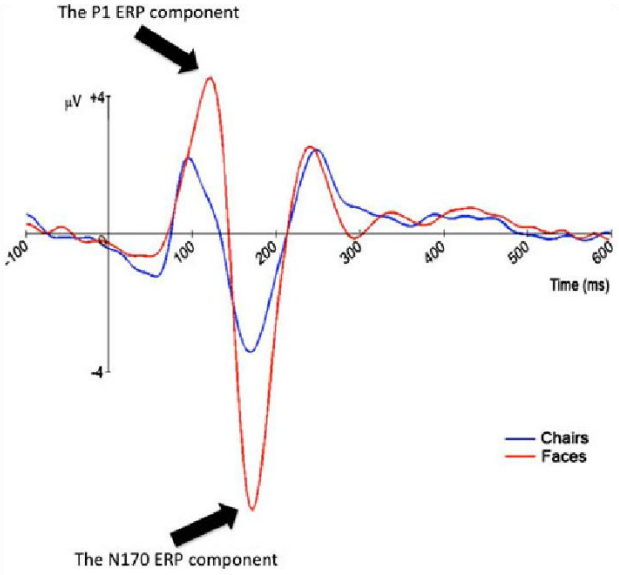
BEST (Biomarkers, EndpointS & other Tools) Resource http://www.ncbi.nlm.nih.gov/books/NBK326791/

CDER Biomarker Qualification Program



https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/biomarker-qualification-program

Biomarker Development for Regulatory Use

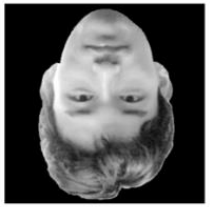


N170: Latency of Peak Neural Response to Visual Presentation of Human Face on EEG

- Accepted into CDER Biomarker Qualification Program
- Context of Use
  - Reduce heterogeneity within the diagnosis of Autism Spectrum Disorder (ASD)
  - Enrichment of clinical drug development trials
- Need to understand how the subgroup differs from other ASD patients

Upright face

Inverted face



Oculomotor Index of Gaze to Human Faces on Eye-tracking Device

Summary

- Biomarkers can be integrated into drug development for psychiatric conditions both through the drug approval process and the biomarker qualification program
- Use of biomarkers in study population selection, stratified randomization, or statistical analysis has potential to improve detection of a treatment effect

Resources

- BEST (Biomarkers, EndpointS & other Tools) Resource http://www.ncbi.nlm.nih.gov/books/NBK326791/
- CDER Biomarker Qualification Program https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/biomarker-qualification-program
- CDRH Medical Device Development Tools Qualification https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt#qualification