APPENDIX
to
Miller JE et al., "Measuring Clinical Trial Transparency: An Empirical Analysis of Newly Approved Drugs and Drug Companies"

CONTENTS:

Appendix 1: List of Analyzed Registries and Data Sources, Including World Health Organization (WHO) Indexed, International, National, and Corporate Registries

WHO International Clinical Trials Registry Platform (ICTRP), which includes the following:	**Location**
1. Association of Clinical Trials Organizations (ACTO)	Russia
2. Australian New Zealand Clinical Trials Registry (ANZCTR)	Australia/New Zealand
3. Brazilian Clinical Trials Registry (ReBec)	Brazil
4. Chinese Clinical Trial Registry (ChiCTR)	China
5. Clinical Research Information Service (CRiS), Republic of Korea	Korea
6. Clinical Trials.gov	United States
7. Clinical Trials Registry - India (CTRI)	India
8. Cuban Public Registry of Clinical Trials (RPCEC)	Cuba
9. EU Clinical Trials Register (EU-CTR)	European Union
10. German Clinical Trials Register (DRKS) (Affiliated registry: DRKS)	Germany
11. International Standard Randomised Controlled Trial Number (ISRCTN.org)	Global
12. Iranian Registry of Clinical Trials (IRCT)	Iran
13. Japan Primary Registries Network (JPRN)	Japan
14. The Netherlands National Trial Register (NTR)	Netherlands
15. Pan African Clinical Trial Registry (PACTR)	Africa
16. Peruvian Registry of Clinical Trials (through PAHO)	Peru
17. South African National Clinical Trial Register	South Africa
18. Sri Lanka Clinical Trials Registry (SLCTR)	Sri Lanka
19. Tanzania Clinical Trials Registry	Tanzania
20. Thai Clinical Trials Registry (TCTR)	Thailand

Other Registries, Databases, and Websites	**Website**
21. ClinicalTrials.gov	www.Clinicaltrials.gov
22. EU Clinical Trials Database (EudraCT)	https://www.clinicaltrialsregister.eu/ctr-search/search
23. Drugs@FDA.gov	Drugs@FDA.gov
24. Aggregate Analysis of ClinicalTrials.gov database (AACT)	https://www.ctti-clinicaltrials.org/aact-database
25. PubMed	
26. Google Scholar	
27. EMBASE	
28. Corporate Press Releases	
Corporate Registry/Website	**Link**
29. Actavis	http://www.allergan.com/research-and-development/clinical-trials/clinical-trial-results-sharing
30. AstraZeneca	http://www.astrazenecaclinicaltrials.com/Submission/Search
31. Allergan	www.allerganclinicaltrials.com/results
32. Amgen	www.amgentrials.com/amgen/study.aspx
33. BMS / DCRI	https://www.dcri.org/soar-data/
34. Celgene	http://www.celgene.com/research-development/clinical-trials/celgene-sponsored-trials/
35. Genentech	http://www.genentechclinicaltrials.com
36. Genzyme (Sanofi)	http://www.genzymeclinicalresearch.com/clinicaltrials/gzcr_p_ot_ourtrials.asp
37. Merck	http://www.merck.com/clinical-trials/search.html
38. Novartis	https://www.novartisclinicaltrials.com
39. Roche	http://www.roche-trials.com/searchFullText.action?drug=2
40. Clinical Study Data Request (CSDR). Includes: Astellas, Bayer, Boehringer Ingelheim, Daiichi-Sankyo, Eisai, GSK, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, ViiV	http://www.clinicalstudydatarequest.com
41. Abbvie	http://www.abbvie.com/research-innovation/clinical-trials-data-and-information-sharing/registration-of-protocols-and-results-reporting.html
42. Janssen	http://www.janssen.com/clinical-trials/transparency
43. Gilead	http://www.gilead.com/research/clinical-trials
44. Pfizer	www.pfizer.com/research/research_clinical_trials/trial_results

Appendix 2: List of Trial Characteristics Abstracted from Registries and FDA Approval Packages

Characteristics: National Clinical Trial (NCT) number, title, recruitment status, whether study results were reported and the date any results were first received, description of the treatment (e.g. dosage and comparators), whether the trial was interventional, sponsors/collaborators, gender enrollment, age groups, phase, enrollment numbers, funder, study type, study design, other IDs, registration date, start date, primary completion date (date the last participant was examined and data for the primary outcome measure collected), primary outcome measures, site locations, and any links to CSRs.

Appendix 3. Additional Information About the Data Collection and Analysis Methods

Data were collected by a team of 5 undergraduate and graduate-level researchers and a PhD-level research director, all of whom were supervised by the principal investigator, Dr. Miller.

Data collectors were trained to read FDA approval packages, use ClinicalTrials.gov and other trial registries, and search PubMed using the search methodology described in Miller et al., 2015.[1] Validated data from drugs approved in 2012 and reported in that article were used as a training dataset. Each data collector's accuracy was tested using a sample from the 2012 data before that person was permitted to move on to collect data for the 2014 sample.

Data for each drug within the sample were collected by at least 2 data collectors, working independently and blinded to one another's work. The researchers then met to validate each other's work and create one master spreadsheet for each drug. If there were discrepancies in the data, they were resolved by consensus of the research group including the principal investigators, sometimes using additional information elicited from the company. Data were recorded, analyzed, and summarized using Microsoft Excel v.15. A list of the data fields extracted are listed in Appendix 2. Many of the variables came directly from ClinicalTrials.gov and Drugs@FDA. We used the NIH data dictionary to define terms.

Data were analyzed by the 2 most experienced data collectors and the PhD-level director, with direction from the faculty investigators. In determining whether a trial met requirements for registration, reporting, publication, public availability, FDAAA applicability, and FDAAA compliance, each analyst reached his/her determination independently of the others. Discrepancies in these determinations were resolved by consensus, with support from the principal investigators. Determination of FDAAA applicability and compliance were made using two primary resources, the Food and Drug Administration Amendments Act of 2007 (FDAAA) and guidance provided by NIH through clinicaltrials.gov information sections on FDAAA.

[1] Miller JE, Korn D, Ross JS. Clinical trial registration, reporting, publication and FDAAA compliance: a cross-sectional analysis and ranking of new drugs approved by the FDA in 2012. *BMJ Open.* 2015;5(11):e009758.

Appendix 4. Details of Validation Process with Drug Companies

To ensure our search process did not miss or mischaracterize facts, NDA holders (generally the manufacturers) of drugs reviewed in the study were sent a copy of their results and the supporting dataset and asked to provide corrections. Companies were also invited to a 3-hour meeting to discuss study methods and findings. Nine of the 11 companies participated in both the meeting and our drug data validation process, affording data validation for 79% of drugs reviewed. Nine additional companies joined the 3-hour meeting.

Corrections were accepted if the research team could corroborate the information with public sources, e.g., by visiting a website to which the company directed us. The scenarios below typify the types of feedback we received:

1) A company indicates that results were reported for a trial on ClinicalTrials.gov, where we marked it as not having results there. We recheck ClinicalTrials.gov, confirm that the results are there, and revise our data. The records on ClinicalTrials.gov are constantly being updated with new information, so occasionally companies submitted information that had not yet appeared publicly at the time of our review.
2) A company clarifies whether FDAAA applies to a particular trial. One requirement for FDAAA coverage turns on manufacturing data, which is difficult to come by through public sources. FDAAA says that a trial must be conducted in the US, or have a drug manufacturer in the US for export, to be covered. In several instances, companies informed us that this requirement was not in fact satisfied, which caused us to correct an initial judgment that the trial was FDAAA-applicable.
3) The company provides a web link to a publication, where we had found no publications. Matching trial characteristics to publications can be challenging, especially for phase 1 trials with no registration record, so some publications were initially missed.

After validation, the median number of trials per drug with publicly available results increased from 90% to 96% in the trials-in-patients sample and from 60% to 68% for all trials. FDAAA compliance increased from 51% to 71% for the "trial completion date" interpretation and from 88% to 100% for the "approval date" interpretation.

Scores changed primarily because the validation process located additional, publicly verifiable journal publications (n=23) and identified typographical errors in FDA approval packages or ClinicalTrials.gov (n=17). Additionally, results for 2 more trials were found in ClinicalTrials.gov (the registry had delayed the postings) and 1 trial was removed from the FDAAA trials sample because the manufacturer attested that the drug was not manufactured in the U.S.

Appendix 5. Information about the Pharmaceutical Executive Roundtable Meeting

On August 17, 2016 and March 10, 2017, the research team hosted Pharmaceutical Executive Roundtables. The first was held at the NYU School of Medicine offices of the Alexandria Center for Life Science in New York City. The second meeting was held at Ernst & Young in New York City. Both meetings had more than 30 participants. The below institutions participated in at least one of the two meetings:

- Representatives from AbbVie, AstraZeneca, Bayer, Biogen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Johnson & Johnson, Lilly, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, and Syndax;
- Bioethics International research staff and Board of Directors members;
- Academic collaborators on the Scorecard project, based at Harvard University, Stanford University School of Law, Yale School of Medicine, and NYU School of Medicine);
- Representatives from the Laura and John Arnold Foundation, Gates Foundation, and Helmsley Foundation, and
- Representatives from Ernst and Young.

The pharmaceutical company representatives had various job titles, such as Vice President and Head of U.S. Medical Affairs, Director of Clinical Trial Transparency, Chief Medical Officer, Chief Executive Officer, and Global Head of Patient Affairs and Policy.

The 2016 Roundtable offered participants the opportunity to learn about the Good Pharma Scorecard's history, methods, and how to comply with its standards. Additionally, participants could candidly discuss concerns with, and provide feedback on, the study team's methodological approach to data collection and analysis. Moreover, participants were encouraged to discuss challenges and barriers to registering and reporting results of clinical trials and publishing the results of trials in medical journals. Root causes of best and inferior practices were also explored.

Each meeting lasted approximately 3 hours and included discussion about the importance of disclosing phase 1 trial results and interpretations of FDAAA's legal requirements for disclosure.

The principal changes to methods in the Scorecard made after the Roundtable were as follows:

- Expanding our search to include international and corporate registries (in addition to registration at ClinicalTrials.gov); and
- Including the clinical study report synopsis as a measure of results reporting.

Appendix 6: List of FDA 2014 Approved Indications for Evaluated Drugs

Drug Name	Short Indication	Indication	Generic Name
Belsomra	Insomnia	indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance	Dasabuvir Sodium; Ombitasvir; Paritaprevir; Ritonavir
Cerdelga	Gaucher Disease	indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test	Dalbavancin Hydrochloride
Dalvance	Skin Infection	indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI), caused by susceptible isolates of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant strains), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus) and Enterococcus faecalis (vancomycin susceptible strains)	Dapagliflozin Propanediol
Esbriet	Pulmonary Fibrosis	indicated for the treatment of idiopathic pulmonary fibrosis (IPF)	Olaparib
Farxiga	Type 2 Diabetes	indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	Naloxegol Oxalate
Harvoni	Hepatitis C	indicated with or without ribavirin for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1, 4, 5, or 6 infection	Dapagliflozin Propanediol; Metformin Hydrochloride
Invokamet	Type 2 Diabetes	indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing metformin or canagliflozin, or in patients who are already treated with both canagliflozin and metformin	Apremilast
Jublia	Onychomycosis	indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes	Efinaconazole
Lynparza	Ovarian Cancer	indicated as monotherapy in patients with deleterious or suspected deleterious germline BRCA mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy	Ledipasvir; Sofosbuvir
Movantik	Constipation	indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain	Idelalisib
Otezla	Arthritis; Psoriasis	indicated for the treatment of adult patients with active psoriatic arthritis; indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy	Canaglifflozin; Metformin Hydrochloride

Sivextro	Skin Infection	indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus Group (including Streptococcus anginosus, Streptococcus intermedius, and Streptococcus constellatus), and Enterococcus faecalis	Suvorexant
Viekira Pak	Hepatitis C	indicated for the treatment of patients with genotype 1 chronic hepatitis C virus (HCV) infection including those with compensated cirrhosis	Tedizolid Phosphate
Xigduo XR	Type 2 Diabetes	indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both dapagliflozin and metformin is appropriate	Ceftolozane Sulfate; Tazobactam Sodium
Xtoro	Otitis Externa	indicated for the treatment of acute otitis externa (AOE) with or without an otowick, caused by susceptible strains of Pseudomonas aeruginosa and Staphylococcus aureus in patients age 1 year and older	Vorapaxar Sulfate
Zerbaxa	Urinary & Abdominal Infections	indicated for the treatment of patients 18 years or older with the following infections caused by designated susceptible microorganisms: Complicated Intra-abdominal Infections, used in combination with metronidazole; Complicated Urinary Tract Infections, including Pyelonephritis	Finafloxacin
Zontivity	Thrombotic Cardiovascular Events	indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD). ZONTIVITY has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, stroke, and urgent coronary revascularization (UCR)	Ceritinib
Zydelig	Leukemia	indicated, in combination with rituximab, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) for whom rituximab alone would be considered appropriate therapy due to other co-morbidities	Pirfenidone
Zykadia	Lung Cancer	indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib	Eliglustat Tartrate

Appendix 7: List of Key Trial and NDA Sponsors for Analyzed Drugs[†]

Drug --> NDA holder --> Registered Trial Sponsor	No. Trials in NDA	Source
Belsomra		
Merck, Sharp & Dohme Corp.	37	Drugs@FDA
Merck Sharp & Dohme Corp.	9	ClinicalTrials.gov
Not Registered	28	N/A
Cerdelga		
Genzyme Corp/Sanofi	17	Drugs@FDA
Genzyme, a Sanofi Company|Sanofi	7	ClinicalTrials.gov
Not Registered	10	N/A
Dalvance		
Durata Therapeutics Inc/ Allergan plc	22	Drugs@FDA
Durata Therapeutics Inc., an affiliate of Allergan plc	2	ClinicalTrials.gov
Pfizer	1	ClinicalTrials.gov
Vicuron Pharmaceuticals	1	ClinicalTrials.gov
Not Registered	18	N/A
Esbriet		
Genentech / Roche Holding AG	21	Drugs@FDA
Genentech, Inc.	4	ClinicalTrials.gov
InterMune	2	ClinicalTrials.gov
Marnac, not registered	4	Personal Communication with NDA holder
William Gahl, M.D.|National Human Genome Research Institute (NHGRI)|National Institutes of Health Clinical Center (CC) (Investigator Initiated	1	ClinicalTrials.gov, Personal communication with NDA holder
Investigator initiated	1	Personal Communication with NDA holder
Not Registered	9	N/A
Farxiga		
Astrazeneca	63	Drugs@FDA
AstraZeneca	17	ClinicalTrials.gov
AstraZeneca|Bristol-Myers Squibb	22	ClinicalTrials.gov
AstraZeneca|Bristol-Myers Squibb|The TIMI Study Group|Hadassah Medical Organization	1	ClinicalTrials.gov
AstraZeneca|Parexel|Q2 solutions|PRA Health Sciences|Covance Laboratories, Inc	1	ClinicalTrials.gov
AstraZeneca; Bristol-Myers Squibb co-sponsor	7	Personal Communication with

		NDA holder
Not Registered	15	N/A
Harvoni		
Gilead Sciences	68	Drugs@FDA
Gilead Sciences	35	ClinicalTrials.gov
National Institute of Allergy and Infectious Diseases (NIAID)|National Institutes of Health Clinical Center	1	ClinicalTrials.gov
Not Registered	32	N/A
Invokamet		
Janssen / Johnson and Johnson	42	Drugs@FDA
Janssen Research & Development, LLC	16	ClinicalTrials.gov
Janssen Research & Development, LLC|The George Institute for Global Health, Australia	1	ClinicalTrials.gov
Janssen Scientific Affairs, LLC	1	ClinicalTrials.gov
Janssen-Cilag International NV	1	ClinicalTrials.gov
Johnson & Johnson Pharmaceutical Research & Development, L.L.C.	14	ClinicalTrials.gov
Mitsubishi Tanabe Pharma Corporation	4	ClinicalTrials.gov
Not Registered	5	N/A
Jublia		
Dow Pharmaceutical Sciences / Valeant	9	Drugs@FDA
Dow Pharmaceutical Sciences	3	ClinicalTrials.gov
Not Registered	6	N/A
Lynparza		
Astrazeneca	28	Drugs@FDA
AstraZeneca	19	ClinicalTrials.gov
AstraZeneca|British Columbia Cancer Agency	1	ClinicalTrials.gov
AstraZeneca|European Network of Gynaecological Oncology Trial Groups (ENGOT)|Myriad Genetic Laboratories, Inc.	1	ClinicalTrials.gov
AstraZeneca|KuDOS Pharmaceuticals Limited	4	ClinicalTrials.gov
AstraZeneca|Myriad Genetic Laboratories, Inc.	1	ClinicalTrials.gov
Not Registered	2	N/A
Movantik		
Astrazeneca	20	Drugs@FDA
AstraZeneca	16	ClinicalTrials.gov
AstraZeneca|Nektar Therapeutics	1	ClinicalTrials.gov
Not Registered	3	N/A
Otezla		

Celgene Corp	30	Drugs@FDA
Celgene Corporation	16	ClinicalTrials.gov
Not Registered	14	N/A
Sivextro		
Cubist Pharmaceuticals / Merck and Co.	21	Drugs@FDA
Trius Therapeutics LLC	18	ClinicalTrials.gov
Trius Therapeutics LLC|Bayer	1	ClinicalTrials.gov
Not Registered Bayer	2	Personal Communication with NDA holder
Viekira Pak		
AbbVie	65	Drugs@FDA
Abbott	3	ClinicalTrials.gov
AbbVie	7	ClinicalTrials.gov
AbbVie (prior sponsor, Abbott)|AbbVie	13	ClinicalTrials.gov
Not Registered	42	N/A
Xigduo XR		
Astrazeneca	26	Drugs@FDA
AstraZeneca	6	ClinicalTrials.gov
AstraZeneca|Bristol-Myers Squibb	15	ClinicalTrials.gov
AstraZeneca|Bristol-Myers Squibb|The TIMI Study Group|Hadassah Medical Organization	1	ClinicalTrials.gov
Not Registered	4	N/A
Xtoro		
Alcon Research / Novartis	4	Drugs@FDA
Alcon Research	2	ClinicalTrials.gov
Not Registered	2	N/A
Zerbaxa		
Cubist Pharmaceuticals / Merck and Co.	14	Drugs@FDA
Cubist Pharmaceuticals	6	ClinicalTrials.gov
Not Registered	8	N/A
Zontivity		
Merck, Sharp & Dohme Corp.	27	Drugs@FDA
Merck Sharp & Dohme Corp.	4	ClinicalTrials.gov
Merck Sharp & Dohme Corp.|Duke Clinical Research Institute	1	ClinicalTrials.gov
Merck Sharp & Dohme Corp.|The Thrombolysis in Myocardial Infarction Study (TIMI) Group	1	ClinicalTrials.gov
Merck Sharp & Dohme Corp.|The TIMI (Thrombolysis in Myocardial Infarction) Study Group|Duke Clinical Research Institute	1	ClinicalTrials.gov

Not Registered	20	N/A
Zydelig		
Gilead Sciences	24	Drugs@FDA
Gilead Sciences	14	ClinicalTrials.gov
Not Registered	10	N/A
Zykadia		
Novartis Pharmaceuticals	13	Drugs@FDA
Novartis Pharmaceuticals|Novartis	9	ClinicalTrials.gov
Not Registered	4	N/A

† Multiple parties can be involved in a drug's development. This table lists the NDA sponsor and individual trial sponsors for each drug we reviewed. Trial sponsors were identified from ClinicalTrials.gov, unless stated otherwise in the table.