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The critical role of academic clinical trials in pediatric cancer drug approvals

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The Critical Role of Academic Clinical Trials in Pediatric Cancer Drug Approvals: Design, Conduct, and Fit for Purpose Data for Positive Regulatory Decisions

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abstract

PURPOSE For decades, academic clinical trials consortia have collaborated to optimize outcomes for childhood cancers through evaluating incremental improvements in conventional mutimodality treatment regimes. There are now increasing opportunities to partner with industry to test new medicines in academic-sponsored trials, but these collaborative studies rarely contribute to marketing authorizations. We addressed why this is the case and sought solutions to enable academic-sponsored trials to directly contribute to the licensing of new medicines.

METHODS Under the auspices of the multistakeholder platform ACCELERATE, we convened a working group of representatives from clinical academia, pharmaceutical industry, European Medicines Agency, US Food and Drug Administration, and patient advocacy to define the challenges and propose recommendations to facilitate academic-sponsored trial design and conduct to be aligned to both the needs of the pharmaceutical company who own the asset and the expectations of the regulatory (licensing) authorities.

RESULTS We identified that although academic consortia have long-standing expertise to conduct robust clinical trials, there were critical gaps in knowledge, standard procedures, and resources that hindered the trial data directly contributing to marketing authorization applications. We propose a suite of recommendations focused on (1) essential documents, (2) essential data, (3) data management, and (4) trial resources, specifically aimed at enabling academic-industry partnerships to deliver an academic-sponsored trial that meets the requirements for a marketing authorization submission. These recommendations pivot around transparency in academic-industry partnerships and early engagement with regulators.

CONCLUSION Academic sponsors and industry partners need to prospectively recognize when the planned collaborative trial could contribute to an application to marketing authorization and plan accordingly. Transparent collaboration and knowledge sharing between the partners opens an important pathway for accelerating new treatments into clinical practice for children with cancer.

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INTRODUCTION

The development of effective treatments for children with cancer has long been a focus of academic pediatric oncologists and a matter of strong international academic collaboration. Disease-focused academic consortia have been very successful in conducting multiagent and multimodality clinical trials aiming to optimize frontline and salvage treatment regimens. Because of this collaborative effort and despite the rarity of occurrence of individual types of pediatric cancers, overall survival rates for children are reaching 80%[1,2] in the developed world. Nevertheless, therapies for children with rare, recalcitrant cancer types, high-risk subgroups, and those with metastatic disease remain suboptimal, and there is a lack of curative salvage therapies following relapse for most cancers in children and young adults.[2-11] Outstanding advances resulting from molecularly targeted cancer drug development and immunotherapeutics have been observed in the past decades, many of which are becoming standard of care for cancer in adults. Despite changes in both the European and American legislation aiming to promote drug development for children,[12,13] availability of approved or licensed new drugs for the treatment of cancer in children still lags significantly compared with cancer drug approval in adults. A recent (2007-2017) survey found only six out of 117 (5.1%) of relevant oncology drugs had an initial approval that included children.[14] The pathway from therapeutic innovation to clinical adoption is traditionally dependent upon the pharmaceutical industry that owns the assets. In pediatric oncology, academic consortia dominate the childhood cancer trials landscape and only 25% of interventional cancer trials

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Despite positive changes in the European and American legislation promoting drug development for children, availability of licensed new drugs for pediatric cancers remains suboptimal. Clinical trials in pediatric cancer are predominantly driven by academic consortia but are increasingly conducted in collaboration with industry to evaluate novel therapeutics. There are perceived barriers inhibiting academic-sponsored trials being accepted for by regulatory authorities as pivotal or supporting trials for a marketing authorization.

Knowledge Generated

Academic consortia are well placed to collaborate with industry to efficiently deliver clinical trials that can directly contribute to marketing authorization submissions. The critical knowledge gaps, particularly in requirements for (1) essential documents, (2) essential data, (3) data management, and (4) trial resources, can be addressed through transparent academic-industry partnerships and early engagement with regulators.

Relevance

There is considerable potential to accelerate the marketing authorization pathway for clinical drug development in pediatric cancer through academia-sponsored, industry-collaborative clinical trials

recruiting patients 0-17 years old (clinicaltrials.gov database 2000-2020) involve an industry partner.

However, there are increasing opportunities for academic-sponsored studies to generate efficacy and safety data on new therapeutics that could directly contribute to a regulatory application for a new or amended label for a medicinal product. Specifically, the data on the safety and efficacy of a new medicinal product evaluated in an academic-sponsored trial should contribute to the total data package, at least as supportive evidence, if not pivotal, submitted by industry to the regulatory authorities responsible for granting marketing authorization and approval, such as the European Commission, following an opinion from the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA). The challenge is that these trials are not typically initiated or conducted with such an intention; therefore, the data generated may not meet all the benchmarks expected by the pharmaceutical company and required by the regulatory agencies. Although there are examples where academic-sponsored studies have been successfully used as pivotal or supporting trials for licensing applications, that is, the development history for dinutuximab,[15,16] this is not typical. The path to approval of dinutuximab also exemplifies the inherent challenges, with pharmaceutical companies often requiring substantial financial and human resource investment to ensure the data are fit for filing (FFF) or alternatively undertake a subsequent industry-sponsored trial to verify the trial outcomes. Both scenarios incur substantial additional resource investment and unnecessary delay in reaching the desired end point, namely bringing a new effective treatment into clinical practice for pediatric patients. In the planning stage of an academic-sponsored clinical trial, where there is collaboration with a commercial partner to supply a medicinal product, there should be careful consideration of the potential for the outcome of the trial to contribute to a new or amended licensed use of the medicine being evaluated. Not all early-phase or new trials will likely be appropriate or even needed for FFF. The consideration of FFF should be based on the goals of the trial, what other studies are underway or planned, the patient population and how they were selected, the proposed end points, and many other variables. The important issue is that this thought process should be considered at the time of trial development, not after the trial has been initiated or completed. This raises the question of what are the roadblocks that impede academic-sponsored trials being able to deliver data that meet not only the requirements of International Council for Harmonisation (ICH) of technical requirements for registration of pharmaceuticals for human use guidance on Good Clinical Practice (GCP) but can also withstand the full evaluation by the regulatory authorities and therefore can directly contribute to the successful review of regulatory submissions?

We convened a FFF Working Group, under the auspices of the multistakeholder platform ACCELERATE,[17] to define the challenges and propose recommendations to facilitate academic-sponsored trial design and conduct to be aligned to both the needs of the pharmaceutical company who own the asset and the expectations of the regulatory authorities should the trial data be sufficient to support an application. The ACCELERATE FFF Working Group included representatives from clinical academia, pharmaceutical industry, EMA, FDA, and patient advocacy, and consulted for specific expertise in trial data management and trial data repurposing.

IDENTIFYING KNOWLEDGE AND EXPERTISE GAPS

There are many academic organizations and clinical trial networks and consortia who are conducting pediatric oncology clinical trials throughout Europe and United States

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that have extensive experience in conducting interventional clinical trials. They have well-developed quality management systems and standard operating procedures (SOPs) that are compliant with GCP and adhere to their national regulatory and research ethics requirements. However, consultation with multiple pharmaceutical companies with experience in partnering with academic sponsors revealed fundamental differences between the way academia and industry collect and manage trial data (Table 1). Although both were focused on data quality and integrity, there were substantial differences in the approach to data management plans (DMPs; processes of data collection, monitoring, and cleaning) delivered by academic sponsors and the expectations of the industry partners. Similarly, the documentation of financial disclosures, investigator qualification, and compliance agreements (eg, the FDA form 1,572 for the United States, not mandated in Europe, for which still local regulations apply[18]) were not standard for academic-sponsored trials. Regarding collection of required data elements in case report forms (CRFs), differences exist in what is considered essential for collection, for example, the details on normal ranges of laboratory measurements or individual drug dosages are not normally collected in academic-sponsored trials.

Although data management procedures are core to the conduct of all clinical trials, academic- and industry-sponsored alike, a filing application requires levels of validation and traceability of not just the study data but of the entire process from data collection, data oversight (including query management), risk management, and document management. The accountability, scope, and range of activities involved in all aspects of a study intended for filing are well described in the guidelines of the International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use, but there are different practices and expectations from industry study teams, which exceed what is required for trials in the academic setting (see recommendation 3). Identification of this gap in normal practice within the academic and industry collaboration often occurs too late to conform to the requirements for regulatory filing. Academic investigators and consortia will typically focus on release of trial data via presentations or publications, whereas industry partners target filing applications, either at an interim stage or once the trial is completed. This difference in planned expectations and usage of the study data leads to the different data collection processes, data cleaning, and review strategies between industry and academia, despite no different regulatory threshold on data management processes in that regard. Industry will aim to create extensive data cleaning/data review strategies including cross-functional data reviews (data management, clinical, biostatistics etc) from the study onset up to the point of any major study deliverable. Data snapshots will follow a predefined set of SOPs describing data cleaning procedures, possible ongoing data freeze process, and interim and final lock. Another difference in approach is in the collation of essential documents (see recommendation 1). Described in the International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use E6 (R2) GCP,[19] these documents individually and collectively permit regulatory evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor against the standards of GCP and all applicable regulatory requirements.

Finally, our surveys revealed differences in the approach to essential data, that is, data deemed critical for the evaluation of the safety, toxicity, and efficacy profile of a drug or medicinal product (see recommendation 2). A clear discrepancy exists between the type and completeness of adverse event (AE) data collected in academic- compared

TABLE 1. Knowledge and Expertise Gaps

Sponsor	Academic	Industry
Trials experience	Any, often phase III interventional or noninterventional, registry type trials. Limited, if any experience with intent to file trials	Phase I, II, III, and IV all conducted with an intent to file
Data management	Focus on data quality and integrity with data cleaning focused on primary analysis and publication. Monitoring strategies normally on the basis of the low-risk nature of the trials with limited source data verification	Clear and concise rigorous DMPs with full monitoring fixed data cleaning and data locking strategies
Documentation	Collects what is required to ensure data quality and quality of trial conduct	Documents anything and everything that ensures data quality, researcher qualification, and (financial) independence assuring objectively verifiable trial conduct
AE reporting	Often pragmatic with focus on unexpected or severe AEs	Complete, to meet filing requirement
Communication	Public presentation and publication	Filing application, with minor focus on public distribution of results

Abbreviations: AE, adverse event; DMP, data management plan.

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with industry-sponsored trials. Although some academic sponsors tend toward a pragmatic approach of collecting only severe (grade ≥ 3) or unexpected AEs, industry partners tend to collect all data for a comprehensive ongoing safety data review for benefit/risk assessment, which requires review of all available AE data including Common Terminology Criteria for Adverse Events grade 1-5. ICH E6/part 5 on quality management gives sponsors the opportunity to implement a system to manage quality throughout the trial process and on a clinical trial level on the basis of identified risks critical to ensure human subject protection and reliability of trial results. A risk-adapted approach to the level of safety data collected may be justifiable where the knowledge of the safety profile of the asset being evaluated is more mature, however, would not be appropriate for first in human/first in child studies. An example in this regard is the marketing authorization of Mylotarg, where grade 1 and 2 AE data were not reported from the pivotal trial.[20] If risk-adapted safety data collection is proposed, it should be discussed with regulators before initiation of the study with a focus on the justification for a pragmatic approach in data collection. Any risks associated with this process of safety data reporting should be acknowledged in advance and appropriate mitigation measures including trial monitoring and training implemented.

RECOMMENDATIONS

Although the conduct of clinical trials by academic sponsors may not always consider the additional data, documents, and procedural requirements that are needed for the whole trial package to be suitable for regulatory purposes, the gap does not appear insurmountable. We propose a set of recommendations that would facilitate more effective academic-industry partnerships and enable the results of academic-sponsored trials to satisfy a regulatory obligation or contribute to a submission for marketing authorization by EMA or approval by FDA. The recommendations are complementary to those summarized in the trial preparedness document by European network of pediatric research at the EMA.[21]

General Principles

Defining the type of trial and the nature of the collaboration. A clear understanding by all partners of the intended purpose of the clinical trial is an essential starting point and necessitates a transparent discussion between academic and industry partners on the potential use of the outcome of the trial. Misunderstandings can arise because of different interpretations of the trial terminology to describe the partnership. In Table 2, we propose the following descriptors to clarify this terminology and highlight circumstances where a trial is being conducted with the intention to be FFF.

Early planning and prospective collaboration. Early planning and timely, frequent communication among academic investigators, pharmaceutical industry representatives, and regulators can ensure the most impactful trials are planned and conducted in a manner that is ICH-GCP compliant, answer the most pressing clinical questions for children, and generate data sets that are fit for filling. Plans for academic-industry collaborative trials in the field of pediatric oncology should be prospective in nature rather than retrospective, with upfront and open communication between all stakeholders. Careful planning, with realistic expectations of all parties, will avoid disappointment and failure to meet both clinical end points as well as provide adequate data to perform a benefit/risk assessment that could lead to a new drug approval.

Continuous and transparent communication. Good communication between academic investigators, industry sponsor, and regulators is essential throughout the trial. Regulators not only have an enabling role, for example, to discuss methodologies or aspects around platform trials requiring rediscussion as evidence emerges, but also serve patient safety, ie, in case of major amendments, because of emerging safety issues (Data Supplement, online only). Communication between all stakeholders ensures that study plans are aligned with the medicinal product development and the disease-specific clinical research strategies while also fulfilling regulatory requirements. Academic sponsors and industry partners should at all times be aware and considerate about the agreed to regulatory requirements of the industry partner to the regulatory agency(ies). Early communication between all stakeholders, including patients, parents, and the advocacy community, can help assure that study plans are aligned to clinical and stakeholder intentions, regardless of who will take up the role of sponsor.

SPECIFIC RECOMMENDATIONS

1. Essential Documents

Identifying essential documents. Section 8 of ICH E6[19] outlines the essential documents that a study sponsor should collect and maintain before, during, and following the conduct of a study. Academic sponsors should familiarize themselves with these guidelines when developing a FFF trial to understand which documents should be shared with the industry partner and which additional documents/documentation beyond ICH E6 may be required by regulatory agencies. This is detailed in an FDA guidance document[22] and the EMA guideline on trial master file (TMF) management.[23] It should be noted that there are differences in their requirements, for example, the FDA Form 1572 on financial disclosure is required for trial conduct in the United States, but not in the European Union. All essential documents should have purpose and address a specific need in a clinical trial. The extent of essential documents required in a FFF trial is not always fully appreciated by academic sponsors. Essential documents for the trial could be supplemented or may be

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TABLE 2. Descriptors of Different Types of Trials

Trial Type	Sponsor[a]	Funding Source	Intended Use of Trial Data	Role of Industry	Intended as FFF
Academic trial	Academic	Nonindustry; ie, charity, philanthropy, government competitive funding calls	Publication and to contribute to the evidence base for clinical practice	None	No
Investigator-initiated trial	Academic	Mixed funding from industry and nonindustry sources	Publication and to contribute to the evidence base for clinical practice	Provision of drug ± a contribution to funding	No, but notable exceptions exist
Academic-industry collaborative trial	Academic	Industry	Toward licensing of the asset and academic publication	Provision of drug and full funding of the trial	Yes
Industry trial	Industry	Industry	Toward licensing of the asset	Full responsibility and ownership of the trial	Yes

Abbreviation: FFF, fit for filing.

[a]The sponsor is an individual, company, or an institution that assumes the responsibility for the initiation, management, and/or financing of a clinical trial.

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reduced where justified in advance of trial initiation on the basis of the importance and relevance of the specific documents to the trial (as referenced in ICH E6 (R2)/part 8 and its subsequent tables[19]).

Storing and filing essential documents. In the European Union, academic sponsors are familiar with storage of documentation in the TMF or electronic TMF, thereby documenting the conduct of the trial and supporting evaluation of the quality of the data. Requirements for the TMF are also detailed in ICH E6(R2)[19] and should be maintained in accordance with best practices for regulatory filing. Rigorous version control of all trial-related documents and procedures cannot be overemphasized and should be in place for all partners involved in trial conduct. Storage of trial documentation should provide for document identification, version history, search, and retrieval. In an academic-industry collaborative trial, the responsibilities for holding essential documents should be stated in the contract between the partners, highlighting the division of responsibilities and tasks delegated by the sponsor to the industry partner or a third party. Noting that in Europe and according to ICH, the final responsibility always remains with the sponsor. But according to the new EU clinical trial regulation (Art 71, 72), there is the possibility for contractually agreed delegation or cosponsorship.[24]

2. Essential Data

Relevant essential data identification and capture. Only collecting the data needed to address or meet the trial end points is relevant to all trials, not just FFF. The question of how much is enough data is an ongoing area of discussion across all trials and can be a cause of debate in academic-industry collaborative trials. The amount and detail of patient data captured need to be relevant for the safety and efficacy evaluation of the investigational product of the trial. However, a level of pragmatism is permissible, and is reflected in the new EU Clinical Trial Regulation,[24] allowing a risk-based approach to data collection, which can be applied to safety reporting to fulfill EU regulatory requirements (Art 41). Potential areas of data collection that could be adapted in a risk-based approach could include the level of detail of prior and current concomitant medications, extent of past medical history, and toxicity grades collected. Conversely, increased granularity in areas like toxicity grading would be needed for earlier stages of a drug's clinical development. The justification for a risk-based approach to data collection should be clearly stated in the trial protocol; tailored to the individual study objective. The ICH provides some guidelines on where it might be appropriate to apply this risk-based approach in its E19 guideline.[25]

3. Data Management

Development of a data strategy agreement. To address the data review requirements inherent in FFF trials, an agreement between the academic sponsor and industry partner should be in place to highlight how data collection and review will be handled between the two parties. It would include the management, documentation, and handling of possible data quality issues. An emphasis on robust data cleaning and good documentation practices from the onset of the trial (system-level edit checks, clinical data reviews, and patient profile reviews) should help reduce the addition of late retrospective data reviews, which will only increase the burden on clinical sites via late breaking queries. These strategies should be governed by SOPs that should be in place before trial conduct with the roles and responsibilities clearly defined upfront. Discussion should begin with trial design and protocol development, and it is recommended that industry and trial sponsor collaborate in a due diligence assessment of the processes and data collection tools before being used on a study. Such due diligence should highlight any potential gaps that could create hurdles toward a filing application, such as insufficient data query procedures, data monitoring plans, and quality control (QC) procedures. In addition, a data transfer agreement should be in place before the trial is initiated where the number and timing of data transfers should be clearly defined (test data transfer, and data transfer before deliverables and at the time of deliverable).

Data management plan. The DMP is an important tool for FFF trials, which is not always familiar to academic sponsors but entails a detailed description of how the study data will be managed throughout the study. Paramount to the production of high-quality data that meet the requirements of regulatory bodies is that the DMP has processes aligned with ICH E6(R2) principles. The DMP should provide a high-level description of the database systems in use, the critical data elements to be collected (as documented in the ICH E8(R1) general considerations for clinical studies guidelines), as well as define any external data sources in use (such as imaging data, central *v* local laboratory data). The DMP should further describe coding dictionaries (including version control), data review methodologies and frequency, and data reconciliation (serious adverse events, Biomarker).

Trial databases. All software systems used in trial conduct should be 21 Code of Federal Regulations part 11–compliant (mandatory for United States, and whenever possible in Europe), meaning they are reliable and thus equivalent to paper records as specified in the EMA Qualification Opinion on eSource Direct Data Capture.[26]

Case report form development. We strongly recommend a close partnership between the academic sponsor and industry in codeveloping the CRF, and data cleaning strategy before study initiation. The goal should be to target the critical data needed to meet the primary, secondary efficacy and safety end points. This will minimize the data collection burden and help guide the necessary data-cleaning activities to assure greater data quality and integrity without

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sacrificing the reporting needs. Furthermore, the sponsor should consider the use of open data standards and open communication as captured in the Clinical Data Interchange Standards Consortium, which is striving toward global adaptation of data collection standards for clinical trials[27] as stated in the EMA reflection paper.[28]

Quality control. Data quality can be defined as the absence of errors that matter and can be achieved with robust and documented processes. ICH E8(R1) highlight that quality factors are considered to be critical because, if their integrity were to be undermined by errors of design or conduct, the reliability or ethics of decision making would also be undermined.[29] Industry-sponsored trials generally have predefined QC processes in place to allow the assessment of the overall data quality throughout the course of a study and before each major deliverable (interim, primary, and final analyses). In academic-sponsored studies, the data-cleaning and QC methodologies may not be as exhaustive. Although a risk-based approach may be adopted if appropriate, if the trial is intended as FFF, adherence to specific QC requirements is needed. Of note is the FDA guidance document, the Electronic Source Data in Clinical Investigations,[30] FDA September 2013, which recommends trial site investigators to review and sign off the CRF data before any data being submitted to FDA. The EU GCP Inspectorate Working Group recommends a similar approach.[31] This also applies to other regulatory agencies such as Pharmaceuticals and Medical Devices Agency, Japan. This would apply to any data submitted before a final database lock, but also interim data used for marketing authorization. The aim is to increase trial oversight by site investigators, and sponsors need to consider if their database supports periodic electronic CRF sign off or implement an alternative process to ensure investigator signatures are obtained and tracked.

4. Resources

Transparent expectations and capabilities. The expectations of the academic sponsor and expectations and requirements of the industry partner should be transparent, with full disclosure on the anticipated use of the data at the outset and of the sponsors' obligation toward the regulatory agencies, as this has a significant impact on the conduct of the trial. The academic sponsor needs to be clear on their technical expertise and capabilities, for example, on data standards experience, database development, study monitoring, the data-cleaning processes, and their capacity to meet the expected timelines for the trial. Any cross-functional resources that could more effectively conduct and deliver the trial should be shared between the two parties. Equally, knowledge of the likely envelope of funding from the industry partner will assist the academic sponsor to determine whether delivery of the project within their infrastructure is feasible to satisfy the FFF expectations. Building a team capable of delivering all aspects of a trial to meet the requirements of FFF is not feasible in an ad hoc fashion for a specific trial. A minimal activity and experience level in the team of the sponsor seems advisable.

Experience sharing. There is an opportunity for academic sponsors who are collaborating with industry on FFF trials to share their experiences, particularly with respect to resourcing, trial database development, drug distribution, and monitoring services. We therefore advocate continued and intensified collaboration and knowledge-sharing between academic trial consortia that characterize pediatric oncology clinical trial delivery. Most activities related to running trials that are FFF require investment in highly capable and well-trained personnel. As expanding and contracting academic teams with experienced personnel aiming to satisfy a specific trials requirement seems impractical and costly, we suggest developing stable and permanent teams to alleviate this barrier. Barring any legal/contractual obligations, industry personnel could help reinforce the academic team for the duration of the trial and/or academic staff given access to industry training programs as ways to consolidate the collaboration.

In conclusion, the goal of clinical drug development in pediatric oncology is to provide ready access to new drugs that will improve the likelihood of survival and decrease treatment-emergent side effects. Recent changes in legislation have and will provide opportunities for an increasing number of mandatory or voluntary pediatric development plans that require optimal execution to assure access to promising new therapies to children with cancer. Successful collaboration between industry and academic investigators with early input from regulatory agencies is necessary, and the inclusion of advocate engagement to ensure patient-centric focus is encouraged. In this paper, we formulate some recommendations for the stakeholder partners involved in this collaborative process. All too often, trials have been conducted without consideration of the end goal of marketing authorization of a product for children with cancer, resulting in (1) a cumbersome process of data reuse because of identified deficiencies with (2) a delay of label despite established clinical utility.

Crucial to success is that early in a trial's development and concurrent with developing the study design, plans for data capture and data management are discussed with the industry partner when there is a potential that the study might contribute to a new or amended approval/marketing authorization of the drug. The option provided by ICH and the European clinical trial regulation to adapt a risk-based strategy to define the trial essential data elements to be captured during trial conduct seems to be a valuable tool to conduct trials as efficiently as possible and to avoid delay in data capture and trial completion The development of a DMP template for academic FFF studies, which is agreed by academic sponsors, industry, and regulators, could ensure all study data processes meet standards needed to

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be FFF. We also recognize the need for education of all stakeholders (industry and academia) on the filing procedure and its requirements and will, with the help of the ACCELERATE platform, strive toward an educational resource for all involved. Many good resources are available, but awareness of these resources seems to be variable among involved partners.[22,23,25-29,31,32]

All stakeholders should recognize the mutual benefit and responsibilities of conducting or partnering in trials with a FFF purpose. To equitably provide access to the most effective therapies, transparent communication and collaboration among academic and industry stakeholders is necessary to align priorities and accelerate regulatory approval. Although the ACCELERATE FFF Working Group was primarily focused on trials relevant to pediatric oncology, it is anticipated that the experience and recommendations could be extrapolated to other disease areas.

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B.D.W. and E.B. contributed equally to this work.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Critical Role of Academic Clinical Trials in Pediatric Cancer Drug Approvals: Design, Conduct, and Fit for Purpose Data for Positive Regulatory Decisions

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