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C3PT TOOL

Best Practices for Regulatory Interactions

v 1.0

MRCT CENTER
THE MULTI-REGIONAL CLINICAL TRIALS CENTER OF BRIGHAM AND WOMEN'S HOSPITAL AND HARVARD

ITCC
INNOVATIVE THERAPIES FOR CHILDREN AND ADOLESCENTS WITH CANCER

Blood Cancer United

CHILDREN'S ONCOLOGY GROUP

Purpose and Scope of Tool

Both the FDA and EMA support a collaborative approach amongst all involved key stakeholders to ensure timely paediatric oncology drug development. This tool lays out the types of regulatory interactions available for multi-stakeholder groups with EMA and FDA.

Multi-stakeholder Collaboration

The FDA and EMA strongly support a collaborative approach among all stakeholders (patient advocacy, paediatric oncology scientific community/academia, commercial sponsors, international regulatory authorities) to facilitate timely development of products for paediatric patients with cancer.

Strategies to support collaboration in platform trial development and conduct include:

- **Early and regular communication** between academic sponsors and regulatory agencies (FDA, EMA) prior to initiation of the platform trial to discuss trial design, and as needed during conduct of the platform trial.
- **Transparent and clear communication** with FDA and EMA regarding the status of discussions regarding paediatric drug development or platform trial design/conduct with each regulatory agency. If discordant advice is causing delays, advising the regulatory agencies of the issue at hand may be helpful.
- **Inclusion of representatives** from each stakeholder group in meetings with regulatory agencies (both for academic sponsor meetings and commercial sponsor meetings).
- **Inclusion of information in iPSPs and PIPs** regarding participation in the platform trial and should seek advice from regulatory agencies if there are questions regarding adequacy of the platform trial participation to fulfill regulatory obligations.

EMA Interactions

There are two pathways for regulatory interactions. This is via the **scientific advice (SA) process** (which includes e.g. **qualification advice/opinion, broad scientific advice, medicinal product-specific advices for clinical trials such as protocol assistance**) and the **PIP process**.

The differences in scope between SA and PIP (and modifications thereof) processes and the Clinical Trial Authorisation process according to Clinical Trails Regulation No 536/2014 need to be acknowledged.

TABLE 1: Comparison of Scope

↓ Aspect	EMA Scientific Advice*	EU Paediatric Regulation Paediatric Regulation (EC) No 1901/2006	CTA (Regulation (EU) No 536/2014)
Primary purpose	To provide non-binding guidance on development strategy (quality, non-clinical, clinical)	To ensure paediatric development is planned and conducted towards evidence generation in support of a paediatric indication	To authorise a specific clinical trial in humans
Legal basis	Procedural service by EMA	Legally required under Paediatric Regulation (EC) No 1901/2006	Legally required under CTR 536/2014
Scope focus	Future development plan and evidence generation strategy	Paediatric studies: timing, design, waivers/deferrals	Specific clinical trial protocol and its conduct
Stage in lifecycle	Early to late development	Early development (initiated earliest after adult Phase I (dose finding trials)	Before starting each clinical trial

TABLE 1: Comparison of Scope *(continued)*

↓ Aspect	EMA Scientific Advice*	EU Paediatric Regulation Paediatric Regulation (EC) No 1901/2006	CTA (Regulation (EU) No 536/2014)
Type of questions addressed	Study design, endpoints, comparators, statistical methods	Paediatric indication(s), age subsets, clinical trials, endpoints, formulations, study timelines	Trial design acceptability, safety, IMP quality, risk/benefit
Explicit exclusions from scope	Cannot assess adequacy of full data for CTA/MAA. For scientific advice on clinical trials see ACT-EU.	Handled separately from SA	Does not cover non-interventional trials or non-medicinal interventions
Binding nature	Non-binding (advisory only)	Binding obligations once agreed (must comply)	Legally binding authorisation required to start trial
Decision-making body	N/A—advisory role only	Paediatric Committee (PDCO)	Member States (via coordinated EU process, CTIS)
Geographical scope	EU-wide advice but voluntary	EU-wide requirement linked to MAA	EU-wide harmonised process via CTIS
Output	Written advice letter	PIP decision (including waivers/deferrals)	Authorisation decision (approval/refusal)
Relation to clinical trials	Helps design trials but does not approve them	May require specific paediatric trials	Directly approves or rejects a trial
Key objective	Improve likelihood of successful development	Ensure medicines are studied in children and de-risking marketing authorisation failure	Protect subjects & ensure reliable trial data

*This refers to centralised scientific advice via EMA. There is also the possibility of simultaneous national scientific advises (SNSA – https://www.hma.eu/about-hma/working-groups/eu-innovation-network-eu-in/eu-innovation-network-eu-in.html).

The following is important to consider in terms of sequence of interactions:

The **SA process** can vary in scope, including advice/opinion on methodologies or broad scientific advice, e.g. advice on core platform trial design elements.

It is important to be clear about the scope for initial and subsequent regulatory interactions in context of the objective of the platform. This then drives to whether a specific type of a SA or a qualification advice on a methodology is the best path forward.

To be able to provide value added regulatory advice, context specificity is important, for example defining specific questions related to core platform design element (e.g. patient population, endpoints, etc). Iterative interactions with regulators are needed, which can be via different types of SAs at a national and European level. Plans for initial and follow up advice (e.g. to refine the core elements and as new evidence comes to light) and timing for different (global) interactions are best pre-defined to ensure efficiency.

There is also the opportunity for parallel SA with the clinical trial coordination group (CTCG), which includes the option for asking also questions/advice on clinical trial application (CTA) related issues (https://accelerating-clinical-trials.europa.eu/our-work/consolidated-advice-clinical-trials_en).

Once there is agreement on (core) elements of the platform via specific procedure(s), product specific interactions via a **PIP or modification submission** (as appropriate) would be facilitated.

APPLYING FOR SCIENTIFIC ADVICE

Scientific advice(s) can be submitted by a non-commercial sponsor and is free to charge if it concerns paediatric patients only or if an academic fee waiver has been sought. This contrasts with the PIP application, which must be submitted by the industry sponsor, but can make use of the SA and involve the academic/non-commercial sponsor of the platform along the process.

To prepare and facilitate formal interactions, academic sponsors are always encouraged to reach out informally to respective EMA contacts within the Paediatric or Scientific Advice office or academic workstream (see Contact Detials section below).

FDA Interactions

There are several types of FDA meetings to support paediatric oncology product development. Complex scientific/technical, policy, or regulatory questions are best posed to FDA in either requests for formal meetings or in formal submissions. Traditionally, FDA has taken a collaborative approach to responding to questions included in meeting packages and in submissions. FDA believes that scientific and regulatory recommendations provided during drug development meetings with sponsors typically result in more efficient and robust development programs. Sponsors can request meetings with FDA at any time during drug development, although meetings at key milestones of product development are particularly important. There are several types of FDA meetings as described in TABLE 2, with each having a different intended purpose and timeframe.

TABLE 2: Types of FDA Meetings

Meeting Type	Description/General Purpose	Timeframe	Considerations for Academic-Sponsored Platform Trials
Type A Meetings	Generally intended to discuss issues that must be addressed to enable an otherwise stalled product development program to proceed or to address an important safety issue	Within 30 days of request	Typically requested by the commercial sponsor. Strengthening communication between the FDA and sponsor can help avoid issues that would require a Type A meeting.
Type B Meetings	These meetings occur at pre-defined endpoints during product development. They can occur prior to submission of an IND (pre-IND), during critical points during clinical development (e.g., End of Phase 2, pre-Phase 3, prior to marketing application submission). Meetings requested by sponsors of BTD products are generally Type B meetings, unless another meeting type (such as Type A, Type F, Type D, or a parallel scientific advice meeting) is appropriate.	Within 60 to 70 days of request	Product-specific meetings are generally requested by the commercial sponsor, but academic sponsors may request a pre-IND meeting to discuss platform trial design prior to the original IND submission of the protocol for the platform trial. Other meeting types (such as Type C) may be more appropriate for other platform-design-related issues.
Type C Meetings	A meeting that is not a Type A or Type B meeting regarding the development and review of a product	Within 75 days of request	These meetings would generally be reserved for meetings that do not qualify for another meeting type.
Type F Meetings	Early advice meetings to discuss pediatric development plans	Within 30 days of request	Generally requested by the commercial sponsor to discuss high-level issues related to an initial pediatric study plan subject to FDARA requirements that has not yet been submitted to the FDA.

TABLE 2: Types of FDA Meetings *(continued)*

Meeting Type	Description/General Purpose	Timeframe	Considerations for Academic-Sponsored Platform Trials
Type D Meetings	Focused on a narrow set of issues (no more than 2 focused topics) which could include: • a follow-up question that raises a new issue after a formal meeting • a narrow issue with few associated questions • a general question about an innovative development approach	Within 50 days of request	Type D meetings can promote proactive, collaborative discussion to help identify and mitigate/ troubleshoot potential rate-limiting steps to platform trial design or conduct. These meetings are generally held to discuss issues that require more rapid feedback versus issues that are better addressed through another type of interaction.
INTERACT* meetings	Intended to facilitate IND-enabling efforts for novel products and development programs that present unique challenges in early development before an IND or pre-IND meeting) Appropriate timing is when a sponsor has identified the investigational product to be evaluated in a clinical study and preliminary proof-of-concept studies have been conducted but definitive toxicology studies have not yet been designed and conducted.	Within 75 days	Generally requested by commercial sponsors. May have limited applicability for academic sponsors of platform trials.
Parallel Scientific Advice meeting	Provides mechanisms for review staff from EMA and FDA to concurrently discuss and provide advice to sponsors on key issues related to development of drugs and biological products	Trilateral meeting generally held by Day 65 following FDA receipt of validated meeting package	This process may expedite communication between platform trial sponsors/ EMA/FDA.

***INTERACT = IN**itial **T**argeted **E**ngagement for **R**egulatory **A**dvice on CBER/CDER **P**roduc**T**s

COMMUNICATING WITH THE FDA

Depending on the scope of the issues or sponsor questions, it may be appropriate for sponsors to request advice outside of a formal meeting. The review division Regulatory Project Manager (RPM) is the primary point of contact for communications between a sponsor and FDA during the life cycle of drug development. As a co-leader of the FDA review team, the review division RPM has comprehensive knowledge of the drug and its regulatory history. To streamline communications and have a mutual understanding of the preferences and expectations for sponsor and FDA communications during drug development, FDA recommends that sponsors and FDA RPMs, particularly the review division RPMs responsible for managing the applications, establish a mutually agreeable communication strategy. The communication strategy can be established early in the development program (i.e., around the time of IND submission) and adjusted at any time when there are outstanding issues (e.g., feedback on a new protocol) or modifications to the development program that might warrant more frequent or possibly less frequent interactions. A communication strategy might include the preferred method(s) (e.g., email versus telephone) and frequency of communications and/or approaches for managing information requests and responses (e.g., one request at a time versus bundled requests). As part of a communication strategy, sponsors and FDA should share contact information for alternative backups and the mutual expectations for the timing of responses to inquiries.

For all other sponsor inquiries that are received via telephone, email, or in a formal submission without a prespecified review, the FDA RPM generally strives to acknowledge such communications via telephone or email within 3 business days of receipt by the FDA RPM with an estimated timeline for response to the sponsor's questions. If unexpected complex issues arise during the review of a submission, FDA will provide an answer when it is fully developed, rather than adhering to a timeline when doing so may provide incomplete information to a sponsor. The timing of FDA response may also be negatively affected if the review team experiences an unexpected shift in work priorities or team staffing. In these cases, the FDA RPMs fully intend to keep sponsors apprised of changes to the estimated response timeline.

Facilitating EMA/FDA Regulatory Alignment

The FDA and EMA work together in several ways to help promote international alignment through participation in paediatric cluster calls, other informal discussions under confidentiality agreement, coordinated participation in the respective agency's industry meetings with sponsor permission, and participation in a variety of general meetings and workshops related to paediatric cancer drug development.

Paediatric cluster calls are monthly teleconferences that are held under confidentiality agreement with participating paediatric cluster members (U.S. FDA, EMA, Japan's Pharmaceuticals and Medical Devices Agency (PMDA), Health Canada, Australia's Therapeutic Goods Administration (TGA) and Swiss agency for Therapeutic Products (Swissmedic)). A range of topics may be discussed, including topics related to paediatric development for a specific product and general topics related to drug development for paediatric patients. **Paediatric cluster call discussions can be requested by paediatric cluster members, or by sponsors.** Following a cluster call discussion, high-level action items are shared with product sponsors to let sponsors know that their product was discussed at the Paediatric Cluster and to convey the agreed-upon action.

At their discretion and upon mutual agreement, FDA and EMA may also issue a common commentary to share unofficial, high-level comments reflecting FDA and EMA subject matter expert discussion at the Pediatric Cluster teleconference. The purpose of a Common Commentary is to help medical product sponsors achieve globally harmonized paediatric product development plans.

Commentaries are meant to highlight scientific or regulatory issues where the FDA and EMA are working toward, or have achieved, a harmonized view. Common Commentaries may also provide clarity to sponsors by outlining important areas where the FDA and EMA may be unable to align.

EMA and FDA can discuss the SAs and PIPs via the existing structures of cluster calls. With sponsor permission, FDA routinely invites EMA representatives to participate in meetings to discuss iPSP content, and sponsors can also request participation of EMA at other FDA meetings.

The academic platform trial sponsor and industry should be transparent about their respective intentions with regards regulatory submissions to other jurisdictions and are encouraged to submit simultaneously if possible. The respective agency(ies) can then inform their counterpart about ongoing discussions. This enables close collaboration towards facilitation of global developments.

Contact Details

EMA Scientific Advice: scientificadvice@ema.europa.eu

FDA OCE Peds Oncology Program: OCEPeRC@fda.hhs.gov

FDA Oncology Center of Excellence: FDAOncology@fda.hhs.gov

References

General information on EMA website on medicines development for children with cancer:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/paediatric-medicines-research-development/developing-cancer-medicines-children

Specific information related to Scientific Advice:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance

Specific information related to qualification advice/opinion:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance/qualification-novel-methodologies-medicine-development

Specific information related to scientific advice on clinical trials:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance/parallel-scientific-advice-special-development-aspects-or-product-types

https://accelerating-clinical-trials.europa.eu/our-work/consolidated-advice-clinical-trials_en

Specific information related to PIPs:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/paediatric-medicines-research-development/paediatric-investigation-plans

Specific guidance related to platform trials:

https://www.ema.europa.eu/en/platform-trials-scientific-guideline

https://health.ec.europa.eu/latest-updates/questions-and-answers-complex-clinical-trials-2022-06-02_en

Academic support/ support for non-commercial sponsors:

https://www.ema.europa.eu/en/partners-networks/academia

https://accelerating-clinical-trials.europa.eu/our-work/support-non-commercial-sponsors_en

Collaboration between EMA and FDA:

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/paediatric-medicines-research-development/paediatric-investigation-plans#joint-ema-fda-guidance-10230

https://www.ema.europa.eu/en/documents/other/common-commentary-emafda-common-issues-requested-discussion-respective-agency-emapdco-and-fda-concerning-paediatric-oncology-development-plans-paediatric-investigation-plans-pips-and-initial-pediatric_en.pdf

https://pubmed.ncbi.nlm.nih.gov/34498227/

https://ascopubs.org/doi/10.1200/JCO.20.02152?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

FDA references

https://www.fda.gov/about-fda/cder-offices-and-divisions/office-oncologic-diseases-ood (contains contact information for the various oncology review divisions within the Center for Drug Evaluation).

https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/interactions-office-therapeutic-products

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-sponsors-or-applicants-pdufa-products

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/master-protocols-drug-and-biological-product-development

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fdara-implementation-guidance-pediatric-studies-molecularly-targeted-oncology-drugs-amendments-sec

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-study-plans-content-and-process-submitting-initial-pediatric-study-plans-and-amended

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/best-practices-communication-between-ind-sponsors-and-fda-during-drug-development

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-regulatory-considerations-complying-pediatric-research-equity-act-and

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-under-pediatric-research-equity-act-and-best-pharmaceuticals-children-act

https://www.fda.gov/science-research/pediatrics/international-collaboration-pediatric-cluster

https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology

https://www.fda.gov/media/87478/download

https://www.fda.gov/media/84040/download?attachment (SOPP 80001.6: Procedures for parallel scientific advice with European Medicines Agency)

https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/otp-interact-meetings