First in Human (FIH) trials
The role of the clinical trial office

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Clinical trial office

◎ 1 office manager + 1 deputy office manager + 10 staff members

★ Duties of the clinical trial center
- Billing contracts and costs
- Reception, creation, and management of each document
- Preparation of necessary procedures for conducting clinical trials
- Contact point for sponsors

★ IRB support
- IRB administrative support

For the purpose of efficient and rational support, we assigned various persons in charge to perform the work.

Duties of clinical trial center ①

① Contract procedure

- Negotiation of contract (memorandum) with the client
  - Can our hospital accept this contract?
  - Confirm intention or interpretation that cannot be understood from the text alone.
  - Check if there are excessive demands and negotiate if so.

② Expense procedures

- Cost negotiation, confirmation of billing details, and confirmation of distribution to in-hospital departments
  - Secure the amount of money necessary for establishing a system that allows our medical institution to conduct clinical trials.
  - Proceed with cost negotiations in consideration of contractual suitability.

Duties of clinical trial center ②

③ Maintenance of procedural documents

- Preparation of standard work procedure manuals for clinical trials
  - Standard business procedure manual for clinical trials, etc.
  - IRB standard business procedure manual
  - Standard business procedure manual for digitization of clinical trial procedures

④ Request for review to IRB and delivery of result notification

- Request a review according to the prescribed procedure and deliver the result after the review

Duties of clinical trial center ③

⑤ HP information disclosure, record storage, etc.

- Disclosure of information on clinical trials and proper storage and management of materials
  - ➢ Information on standard business procedure manuals, IRB schedules, and procedures is posted on the website.

※ Disclosure of information necessary for sponsors to select our hospital
→ Reduction of labor required for selection survey
Promotion that helps us get selected

https://www.ncc.go.jp/jp/ncch/division/clinical_trial/info/clinical_trial/professional/index.html

Websites must always be as complete as possible!

IRB office

① Commissioned by a committee member

② Creating committee minutes

③ Committee management

- Assisting the progress of the committee, requesting the committee members to review, and delivering the results

④ Saving records, etc.

Digitization of clinical trial documents from December 2020.

IRB members

➢27 in total

➢External committee members: 5 people

(specialized committee members: 2 people, non-specialized committee members: 3 people)

- Doctor: 1 person, pharmacist: 1 person

➢National Cancer Center staff: 22 people

（Professional committee members: 20 people; non-specialized committee members: 2 people）

- Doctors: 15 people, pharmacists: 3 people, nurses 2 people

※ Doctors are mainly composed of internal medicine doctors, and surgeons also participate
Examining the ethical and scientific validity of clinical trials as a cancer treatment professional

Management of IRB

- The speed of clinical trial procedures is slower than in Western countries.
- There has been a demand for speeding up and improving the efficiency of procedures.
- If the application is held once a month (11 or 12 times/year), there is an adverse effect of delay by one month if the application timing is missed.
- Therefore, we tried to speed up and improve efficiency by holding the application twice a month.

There is no upper limit for review tasks at one committee members meeting, and there is no reservation for review.

The system was set up so that applications could be submitted at an appropriate time and examined promptly.

IRB (achievement)

FY 2021

	April	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Totals
New trials	25	28	15	21	25	27	18	13	22	20	18	15	247
Continuing	66	54	71	73	66	72	76	50	58	67	68	68	789
Changes (reviewed)	292	248	386	313	220	349	268	251	356	298	367	323	3671
Changes (fast-track)	238	185	412	88	61	88	83	78	138	123	108	26	1628
AEs	135	104	184	141	136	183	171	136	122	139	129	106	1686
Safety reports	1405	1093	1574	1196	1156	1481	1177	1196	1190	1437	1455	988	15348
Completed cases	20	18	20	14	9	15	11	17	13	10	16	12	175
Total	2181	1730	2662	1846	1673	2215	1804	1741	1899	2094	2161	1538	23544

Conducting FIH trials

- New trials
- Revision of clinical trial implementation plan, explanation/consent document, etc.
- Serious adverse events that occurred in the hospital
- Safety information provided by the sponsor
- Report of serious deviations that occurred in the hospital

→ It is essential to establish a system that can promptly and appropriately conduct reviews of these processes.

Specific support ①

- New trials
  - ✓Confirmation of application materials
  - ✓Confirmation of the contents of the explanation/consent document

    → Created a template together with CRC based on the contents pointed out by the IRB in the past. When creating a template, ask committee members to confirm the contents as necessary.
  - ✓In the case of the review of the same clinical trial applied at another hospital, the review contents at that time will be shared with the committee members to improve the efficiency of the review and make the review consistent.

- Revision of the clinical trial implementation plan, explanation/consent document, etc.
  - ✓Confirmation of application materials and explanation/consent documents

  ※ Revisions to the study protocol frequently occur.

Specific support ②

- Serious adverse events that occurred in the hospital

Report of serious deviations that occurred in the hospital

✓Confirmation of report contents

→ Check if the content of the report is complete and if the necessary information is included.

→ Feedback to CRC

- Implementation status report

✓Request to create a report

→ Request to prepare according to the time when the report needs to be submitted

✓Request to prepare according to the time when the report needs to be submitted

→ Check if there are any deficiencies in the report content and give feedback to the CRC

Application: notification of review results ①

① Application (clinical trial request form + review documents)

✓review documents・ICF confirmation → feedback if there are any deficiencies

② The head of the medical institution asks the IRB for a review

③ Prior review

✓Each committee member conducts a review based on the review documents ⇒ report the review results

✓If it is on hold, report the opinion on why it is on hold ⇒ present the opinion of the committee members to PI/CRC/requester

✓PI, etc. will respond to the opinions of committee members and revise the materials as necessary.

✓Answers and corrections to committee members ⇒check the contents of the answers and report the review results

Application: notification of review results ②

④ IRB convention

✓Approve after correction ⇒ report the opinion of the committee members to the responsible doctor/CRC/client

⇒ Confirm the content of the opinion, answer, and revise the material if necessary.

⇒ Committee members confirm the contents

⑤ Report IRB results to the head of the medical institution

⑥ The head of the medical institution notifies the client and PI of the result.

Required period: ①-④ 4 weeks ④-⑥ 2-3 days

5 weeks from application to notification of results

IRB day flow ①

1. Confirmation of the required number of people
2. Confirmation of minutes
3. Report on the implementation status of contract research
4. Review

A) Appropriateness of implementation
Review of new issues

} Explained by the investigator

・Outline of the clinical trial
Overview, investigational drug, design, etc.
・Opinions and answers from the prior review

B) Appropriateness of continuation
① Trial continuation
② Changes to implementation plans, etc.
③ Emergency avoidance deviation report
④ Significant deviation report
⑤ Adverse event report (in-hospital)
⑥ Safety report (outside the hospital)
⑦ Physician-led clinical trial monitoring, audit report

} Explained by the clinical trial center

IRB day flow ②

5. Report
   - ① Changes to clinical trial implementation plans, etc.
   - ② Report of completion/cancellation / interruption of clinical trials, etc.
   - ③ Report of development discontinuation, etc.

} Reported by clinical trial office

- Committee members meeting time: about 2 h/meeting
- We place more importance on reviewing the suitability of continuation than the suitability of implementation.
  - ✓ Appropriateness of implementation

  → There are few opinions on clinical trial implementation plans, etc., and many opinions on explanation consent documents.
  - ✓ Appropriateness of continuation

  → There are many opinions on the implementation system and how to respond to the events that have occurred.

IRB committee members opinion

- Appropriateness of implementation
  - ✓ I have the impression that the explanation of the investigational drug is insufficient. It is better to have an explanation of the mechanism of action.
  - ✓ Insufficient description of treatment when not participating in clinical trials.
  - ✓ The word tolerability seems confusing to the general public. Consider easy-to-understand words.

- Appropriateness of continuation
  - ☐ Continuing clinical trials
    - ✓ It seems that there are many deviations due to mistranslation of the clinical trial protocol. What are the causes and countermeasures?
    - ✓ It seems that multiple deviations from biomarker blood sampling have occurred. What are the causes and countermeasures?
    - ✓ It is difficult to obtain consent, but what are the causes and countermeasures?
  - ☐ Serious adverse events
    - ✓ This is an unknown event. Is it judged that the revision of the explanation consent document is unnecessary?

Summary

- Support for conducting ethical and scientific reviews.
- Streamline and speed up clinical trial procedures.
  - ✓ The IRB convenes twice a month
  - ✓ Review support and cost/contract negotiations proceed in parallel
- Establish a system to prevent situations where clinical trials cannot start or progress due to clinical trial procedures.

For our present patients and for the patients that will come after them.