A TALE OF TWO IBCs: ONE UNIVERSITY, TWO IBCs

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Abstract

In institutions with increasing requests for approval of Human Gene Transfer (HGT) clinical trials, it is a challenge for a single Institutional Biosafety Committee (IBC) to review and approve research involving HGT clinical trials while simultaneously reviewing other protocols. At the University of California San Diego (UCSD), the increase in protocol submissions to the Institutional Biosafety Committee (IBC) and the recent change in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) led to the addition of a separate IBC charged specifically to review HGT clinical trials, called the Human Gene Transfer IBC (HGT-IBC). The HGT IBC partners with a clinical biosafety consulting service provider tasked to provide accelerated, compliant reviews of clinical trials. This report will discuss the challenges, lessons learned, and successes in having two independently functioning IBCs in a large academic institution.

Introduction

With the advancing trend in Human Gene Transfer (HGT) in clinical trials, and the recent NIH decision to remove protocol submission, review, and reporting requirements by the Recombinant DNA Advisory Committee (NIH-RAC) [renamed the Novel and Exceptional Technology and Research Advisory Committee (NExTRAC)[2]], Institutional Biosafety Committees (IBC) are tasked to provide biosafety oversight for research categorized under III-C of the NIH Guidelines. It is imperative the IBC develop an expeditious and thorough evaluation process to ensure the safety of those handling, delivering, or potentially exposed to investigational new drugs (IND) which transfer recombinant or synthetic nucleic acid molecules into human participants. Our institution divided the IBC into two IBCs, one with a focus on laboratory research and non-recombinant clinical protocols, known as the Campus IBC, and the second overseeing clinical research involving recombinant or synthetic nucleic acids classified under III-C of the NIH Guidelines, known as the Human Gene Transfer (HGT-IBC). This report highlights the advantages of having two independently functioning IBCs in a large academic institution.

Methodology

In separating the IBC into two committees, it is critically important to define not only the scope of work, but also how the committees interact. The HGT-IBC charge outlines committee responsibility to establish and enforce policies and procedures based on guidance documents from NIH and Food and Drug Administration (FDA). It limits committee oversight to clinical protocols involving human gene transfer (non-recombinant protocols are reviewed by the Campus IBC). The HGT-IBC utilizes a biosafety consulting service, providing accelerated, compliant reviews of clinical trials, expertise, and reduction of administrative burden on the IBC administrative support system. The committee composition incorporates the consulting service, as well as the necessary subject matter experts (campus and community members), with overlap between the two IBCs (Table 1). The Chair of the HGT-IBC continues to sit as a member of the Campus IBC, and the HGT-IBC Biosafety Officer (HGT-IBC BSO) serves on both committees. The HGT-IBC BSO provides regular reports to the Campus IBC in the interest of communication and institutional partnership. The HGT-IBC and Campus IBC are separately registered with the NIH[3].

Committee Composition	
Campus IBC (24 members)	HGT-IBC (11 members)
Chair	Chair
Biosafety Officer (sits on HGT IBC)	Administrative Chair (Consultant)
HGT Biosafety Officer	HGT Biosafety Officer
Plant Expert *(ad hoc)*	Biosafety Officer
Animal Expert	2 Clinical HGT Experts
HGT Chair (*ad hoc*)	2 Consultant Clinical HGT Experts
3 Community Members	2 Community Members
Occupational Health Expert	Occupational Health Expert
Departmental Representative Research Members	

Table 1: Comparison of committee composition of Campus IBC and HGT-IBC (assembled in accordance with NIH Guidelines Section IV-B-2). HGT-IBC has focused expertise on human gene therapy, clinical trials, and occupational health.

Results

Following the separation in 2018 of the Campus IBC into two autonomous committees, the number of protocols reviewed overall and per meeting increased, as did the amount of committee time dedicated to each individual protocol (Fig. 1, Fig. 2). The formation of a dedicated HGT-IBC has seen a net benefit for our institution (Table 2).

Results

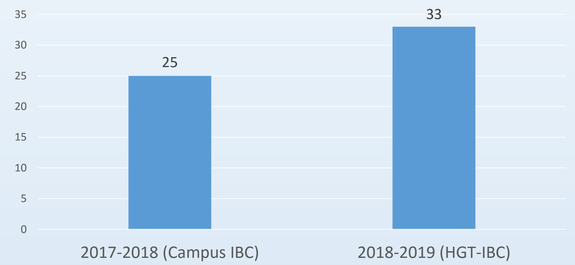

Figure 1: Comparison of number of HGT protocols reviewed for the year by the Campus IBC (2017-2018) to the HGT protocols reviewed by the HGT-IBC after the separation (2018-2019) YTD.

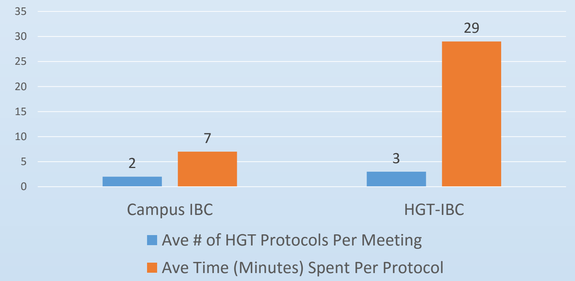

Figure 2: Average number of HGT protocols reviewed per meeting and average time spent reviewing 1 HGT protocol by the IBC per meeting before the separation (Campus IBC 2017-2018) and after the separation (HGT-IBC 2018-2019).

Campus IBC	HGT-IBC	Institutional Benefits
Focused on laboratory research and non-recombinant clinical protocols	Focused on clinical research involving recombinant or synthetic nucleic acids, the bulk of clinical protocols	More protocols reviewed in a 1 month period
600 protocols total	33 protocols total	Protocols reviewed by a greater number of subject matter experts
Increased committee time to biosafety program elements • High Containment • Insectary • Permits (USDA, APHIS, CDC, etc.)	Increased site inspections and committee discussion on clinical facilities	Policy discussion more robust
Consistent committee training	Developed clinical specific training	Higher Committee engagement
Additional time for policy review	Consistent committee training	
	Additional time for policy review	

Table 2: Committee and Institutional benefits as a result of establishing two IBCs.

Conclusion

The vast differences between research and clinical settings, complexity of clinical human gene therapy protocols, and the changing regulatory landscape from FDA, and NIH-RAC triggered a need at our institution for more extensive and expeditious IBC oversight. Time investment is necessary for comprehensive reviews during a convened meeting. For a large institution, such as ours, the 2-hour monthly IBC convened meeting was not providing sufficient time for reviews, IBC training, and other administrative tasks.

Construction of a dedicated HGT-IBC has eased administrative impaction, increased directed expertise, and increased both the number of protocols able to be reviewed and the time dedicated to the reviews. Other administrative tasks such as policy development and training implementation have become standing topics at both committee meetings. The administrative burden from separating the Committees was neutral for campus personnel with the contractor taking the bulk of administrative tasks; protocol support, agenda, meeting minutes, approval letters.

Challenges have included limitations on the pool of potential committee members, the need for more community members, and implementation of processes to ensure both the two committees agree upon major policies. Potential challenges may arise if both committees do not agree concerning a specific IBC/Biosafety policy. In an effort to reduce the potential conflict, membership overlaps between the two committees and a standing agenda item has been created during the Campus IBC meetings, to allow for awareness of the HGT-IBC decisions.

This institution's tale of two IBCs is presented to provide a model for other large academic institutions to better adapt to the ever-changing environment surrounding human gene therapy and its compliance requirements.

References

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