Eastern Michigan University Human Subjects Review Committee: Analysis of Review Times

by

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Abstract

The Eastern Michigan University Human Subjects Review Committee (UHSRC) is the Institutional Review Board (IRB) of Eastern Michigan University. Every research conducted in the university needs to be submitted to UHSRC.

This study was to determine the complete review time of "Eastern Michigan University (EMU) Office of Research Compliance" and to review exempt research submissions for risk and its completeness in the social and behavioral arena and to judge if it functions efficiently. A sample data from Eastern Michigan University's IRB database was collected to analyze the exempt review completion time. The time at each step was collected, analyzed and compared with the average national time collected by Association for the Accreditation of Human Research Protection Programs Inc. Also a review was conducted to judge which party in the process takes the maximum time and what measures can be taken to improve it. Improving this procedure timeline will accelerate the research approvals and efficiency in IRB functioning.

As a national benchmark from AAHRPP it takes a median of 14 calendar days for IRB's to determine exemption for a protocol**.** Results of this study show that EMU UHSRC complete review time was similar to the national average benchmark.

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Introduction

Background

Human subjects in research are protected by two shields, Informed Consent and Institutional Review Boards (IRB). The need of Informed Consent was a result of the Thalidomide tragedy. In 1950 Thalidomide, a sleeping pill was tested in Europe and in the United States. In this trial pregnant women were part of the population, and many children born to these women suffered from phocomelia (shortening of limbs). Thalidomide if taken by women in their first trimester results in limb defects in fetuses. This tragedy led to the Kefauver – Harris Amendments in 1962. As per this amendment two protections are mandatory to run a trial:

1) Signing of Informed Consent from subjects used in drug studies

2) Reporting of adverse event to US Food and Drug Administration (Woodin, 2004)

The National Research Act of 1974, which was passed due to the publicity of an unethical Tuskegee Syphilis study, created the National Commission for the Protection of Human Subjects and Biomedical and Behavioral Research. It also required the establishment of Institutional Review Board (IRB) for all research that received funding from the US government. Later this act was modified to require IRB approvals regardless of funding source. (Woodin, 2004)

The FDA regulations define IRBs as "Any board, committee or group formally designated by an institution to review, approve the initiation of and to conduct review of biomedical research involving human subjects" (US FDA, 2015). The FDA regulations 21 CFR 56 detail all regulations that apply to IRBs. Protection of rights, safety and welfare of human subjects is the fundamental purpose of IRB. There are two types of IRBs: independent and central. Central IRBs are not affiliated with any institution and independent IRBs are.

All Eastern Michigan University (EMU) faculty, staff, and students who are conducting research using human subjects are required to submit an application to the University Human Subject Review committee (UHSRC) for review. All studies must be approved to begin any research activities involving human subjects. Studies are either reviewed by the UHSRC or by a college-level Human Subject Review Committee. The UHSRC exempt review procedures list exact steps and maximum time limit of the process. Submissions are locked by the PI and sent to

the office. Once received by the Office of Research Compliance, they are unlocked and reviewed. If the submission is incomplete or any documents are required, the administrator contacts the PI to complete the package with the needed documents and to relock the package. Once the application package is complete, the research will be preliminarily reviewed for risk. If the research is judged not greater than minimal risk, and all research activities fall into one or more exempt categories then the Office of Research Compliance sends the application to the Chair of the appropriate College Review Committee. The College Review Committee Chair assigns the study to one or two College Level reviewers who have 14 days to complete their reviews. The College Review Committee Chair then reviews, compiles all reviews, and sends correspondence to the PI. If any queries or additional documents are generated during the review then these go out to PI in the correspondence. The response to these revision request letter are processed by the College Level Committee Chair within 2 to 4 days upon receipt. Once all the queries are resolved and the requirements are fulfilled the College Level Committee Chair sends an approval correspondence to PI after which the research activities can begin. (UHSRC Exempt Review Procedures, 2015)

EMU had a manual system of tracking its submissions until August 2014. In September 2014, it started tracking the submissions and approvals in an IRBNet database. The use of IRBNet database coordinated communications and tracked correspondence systematically. It reduced the amount of paperwork and mail, which further reduced the time consumed in clerical work. Due to this database the office staff could concentrate on complicated cases and the review timelines and staff meetings could managed with minimum human error. The process became transparent by giving real-time updates to all the parties (investigators, review teams, chair, etc.).

The research process slows down and resources are wasted if the IRB does not function efficiently. The time taken to review the research and the decisions made after the review may vary across the U.S. IRB's (Larson, Bratts, Zwanziger, & Stone, 2004)**.** The research was done to quantify how the IRB decisions vary on a single protocol. An observational, pediatric research protocol was used for this research. As of the results out of 37 sites initiating the IRB process, 34 (92%) participated in this IRB-approved study. Institutional review boards returned initial applications in a median of 19 days and 91% considered the protocol to be minimal risk. Of 34 submissions, 13 required no changes, 18 received conditional approvals and 3 were deferred. The median time from initial submission to final approval was 42 days. Seven sites did not participate

in patient recruitment - two had institutional issues, one obtained IRB approval too late for participation, and four sites (12%) reported that IRB hurdles contributed to their lack of participation. (Mansbach, Acholonu, and Camargo Jr., 2007) Similar research was done on multi-institutional educational research proposal of medical students' quality life in 6 institutions to analyze and compare how different the IRBs process and evaluate a protocol. As a result of this research, four IRBs determined the protocol was appropriate for expedited review, and the other two required a full review. Also, there was a distinct variation in the time to review the protocol by an IRB member (range 1–101 days) and by the IRB committee (range 6–115 days). One IRB committee approved the study with no changes while the remaining five IRB committees had a median of 13 requests for additional information/changes to the protocol. Sixty-eight percent of requests (36 of 53) pertained to the informed consent letter; one third (12 of 36) of these requests were unique modifications requested by one IRB but not the others. Although five IRB committees approved the survey after a median of 47 days (range 6–73), one committee had not responded six months after submission (164 days), preventing that school from participating.

As the above research results and conclusions proved the variations in different IRB review timelines and decisions, this study results were further compared with the AAHRPP national annual report of IRB review timelines.

Association for the Accreditation of Human Research Protection Programs

The Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) is a non-profit organization that helps to maintain high-quality research through an accreditation process that works with organizations worldwide to strengthen their human research protection programs (HRPPs) by ensuring that HRPPs meet rigorous standards for quality and protection.

The data for the metrics of national benchmark (AAHRPP, 2015) were collected by AAHRPP from the annual reports and new applications of their members in the year 2014. These data were based on the information supplied. AAHRPP has compiled an information database to help research organizations, researchers, sponsors, government agencies, and participants identify and support high-performing practices for HRPPs. The report discusses IRB review times for various research types nationwide. The figures provided by AAHRPP were from sponsors, researchers, and IRBs with objective data to answer such questions as how long it

takes the average accredited institutional review board or ethics committee to move a protocol from submission to approval. In fact, because so many have asked such questions about the research enterprise, without uncovering many evidenced-based answers, AAHRPP updates these charts regularly and adds new data annually.

Purpose:

As IRB complete review time vary affect research timelines and site or Principal Investigator (PI) participation in research, this study was conducted to evaluate the overall time taken by the EMU UHSRC and to compare it to the national benchmark.

Methods

1) Data representative of approved or exempted research submitted to the Eastern Michigan UHSRC were collected from the university database in IRBNet. At the time of data collection, March 2015 was the only month for which representative data were available. The new IRB system was implemented in Sept 2014. It was anticipated that it would take 4 months for users to learn the system; however it took until February 2015 for users to become comfortable with the new system. Since the data before March 2015 were not a reliable or representative sample of current IRB functioning, only data from March 2015 were considered for analysis.

2) The dates of the following 7 steps for each individual case were obtained from IRBNet

   a) Date of submission of the locked package from PI to UHSRC

   b) Date on which EMU's Office of Research Compliance unlocked the package for review

   c) Date when package was received by the chair of the UHSRC for review

   d) Date when the package was received by other reviewers from the chair

   e) Date of correspondence from chair to the PI

   f) Date of response from PI to chair

   g) Date of final decision of exempt or approval

3) The number of days taken to complete each step was calculated by subtracting date of following step from the date of preceding one

4) The total time taken by each individual party, such as PI, UHSRC chair was calculated by adding their respective time taken during the various stages of this process.

5) If the start and end date was same, then it was considered as 0 days for that stage.

6) Various statistical measures such as mean, median, standard deviation (SD) were calculated using above values.

7) With the help of these statistical measures, each step was analyzed for its efficiency with respect to time and descriptive statistics were presented.

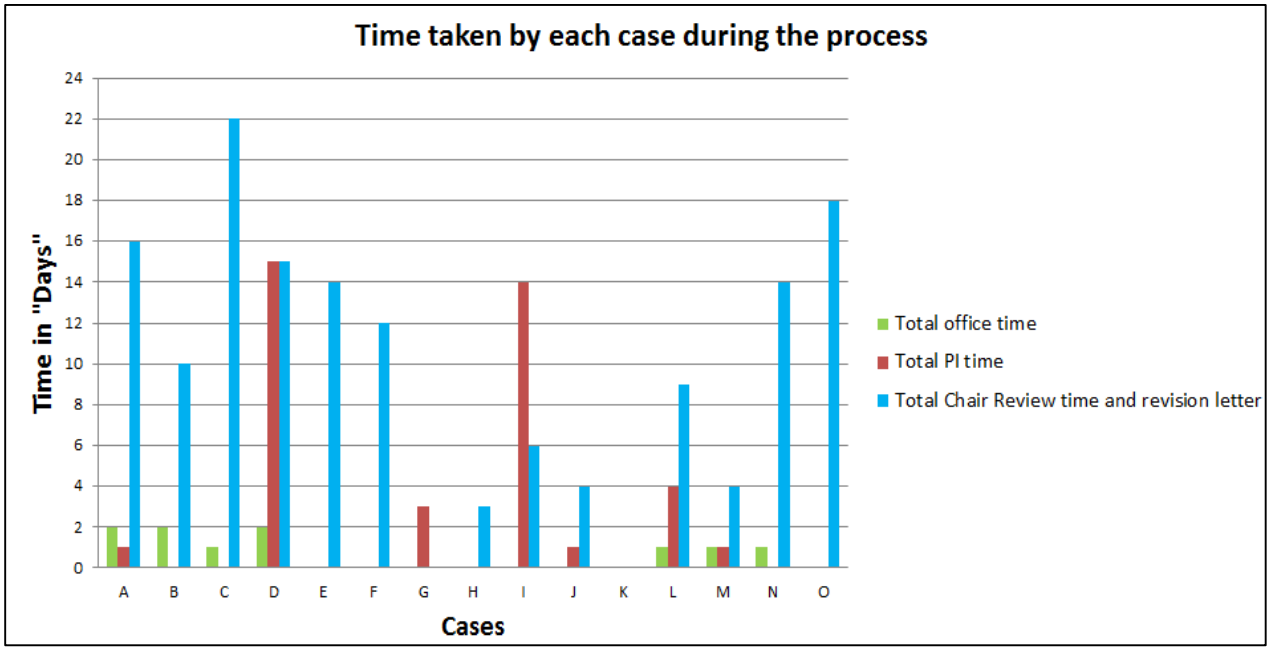
8) The review time was then compared to the AAHRPP benchmarking for the year 2012.

Results

The analysis of fourteen exempt cases (Figure 1) which were found in the IRBNet database during this study displayed that UHSRC's average review time was 15 days with a median of 14 days. The time deviated with a standard deviation of 7.7 with a minimum review of less than 1 day to a maximum review time of 32 days (Table 1).

As of the national benchmark (AAHRPP, 2015) median of 14 calendar days were taken from submission to exempt determination. It took UHSRC a median of 14 days to deem protocol as exempt during the time of the study

Figure 1. **Graph of turnover time (each representative case)**



Total office time-	Total time taken by office to review and unlock or forward package to chair reviewer
Total PI time-	Total time taken by PI To complete the revisions and respond to all correspondence
Total Chair Review time and revision letter-	Total time taken by chair to complete review and all correspondence

Note: If the start and end date is same, then it is considered as 0 days for that stage

Table 1. **Summary Statistics**

	Total office time	**Total PI time**	**Total Chair Review time and revision letter**	**Total time for Approval/Exempt**	**Total Reviewer time**
Mean	1	3	10	15	8
Median	0	0	10	14	9
SD	0.8	4.9	6.7	7.7	5.7
Min	0	0	0	0	0
Max	2	15	22	32	15
95% CI	(0.25, 1.08)	(0.08,5.12)	(6.37,13.23)	(10.73,18.6)	(4.82,11.35)

Discussion

In comparison to the national data collected by the AAHRPP and the Exempt Submission Processing review timelines as referred in the UHSRC Exempt Review Procedures on EMU Research website, the EMU IRB exempts were provided in timely manner.

The average time taken by the Office of Research Compliance to verify the investigator's application package and to forward it to the UHSRC chair for review was 1 day and that of the chair`s time to review and send out correspondence to the PI was 10 days. The duration of the chair review and correspondence was within the expected timeline of 18 days as referred under UHSRC exempt review procedures (14 days of committee review and 4 days of correspondence from chair to PI after the response from PI on revision letter) and shows that the overall approval or exempt process timelines were within expectations.

Total time for Approval or Exempt Decision

The total time taken to approve or exempt the 14 cases varied from less than 1 day (min = 0) to 32 days. This resulted into a standard deviation of 7.8 indicating completion time dispersing widely from its mean of 15 days. This may be explained by case "D" and case "K" (see Appendix).

Case K was provided an exemption on the submission day while case D took 32 days from its submission (Figure 2). For both cases no other reviewers except the chair reviewed the submission. For case K neither revision nor package unlock occurred but for case D the package was unlocked twice and PI took 15 days to update the unlocked package. The office took a total of 2 days to unlock the package and the chair took 15 days to complete the review of the submission. After the package was sent to the Chair, no interactions occurred. The Chair solely took complete 15 days to approve.

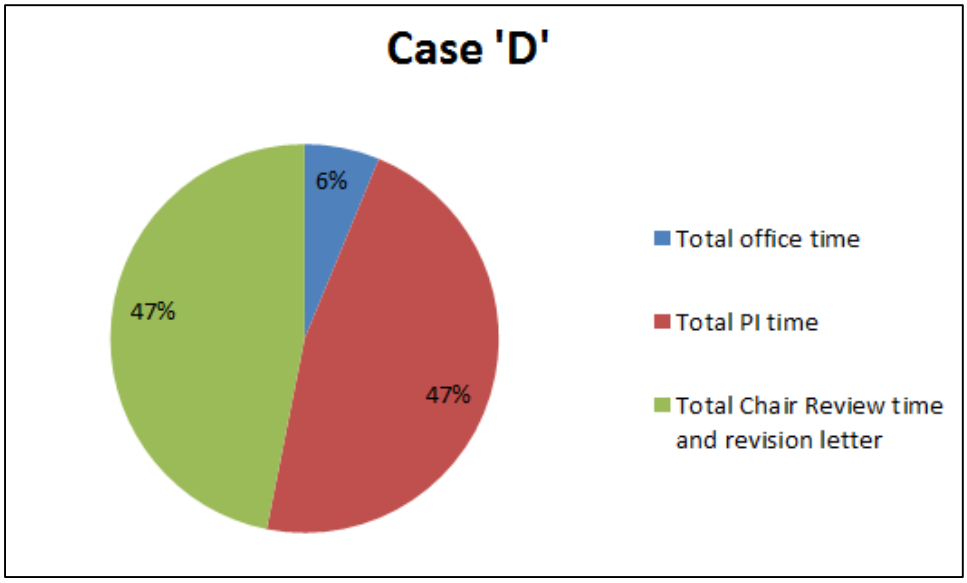


Figure 2. **Case with maximum day turnover**

Total office time

Total office time is the time taken by the office to review supplementary documents and check that all required documents are in package. The total time taken by the office to review the package was less than 1 day (min = 0) to 2 days. In most of the cases office responded within a day's time to the PI or has forwarded the submission to the respective chair. The Office unlocked package or acknowledged on the same day. There are three cases where the office took more than a day to send submission to the chair (Table 2).

Table 2.**Step-by-step turnover of supplementary document review**

Case	Submission notification	Package unlocked 1	Office time 1	Revision complete 1	PI time 1	Package unlocked 2	office time 2	Revision complete 2	PI time 2	Acknowledgement (sent to Chair)	Total office time
A	6-Mar-15	N/A	0	N/A	0	N/A	0	N/A	0	8-Mar-15	2
B	6-Mar-15	N/A	0	N/A	0	N/A	0	N/A	0	8-Mar-15	2
D	9-Mar-15	10-Mar-15	1	15-Mar-15	5	16-Mar-15	1	26-Mar-15	10	26-Mar-15	2

In case A and B the submission was done on 06/Mar/2015 and the chair acknowledgement went out on 08/Mar/2015. (Note: 06/Mar/2015 was Friday)

Case D the office took total 2 days to complete its procedure. However, there were 2 revisions to the package. The submission occurred on 09/Mar/2015. The office unlocked the package in one day for revision 1 and then again took 1 day to unlock the package for 2nd revision.

The PI average time taken to get back with updated documents or to send a response to the chair was 3 days. Although some of the cases have taken extra time, the mean indicates that it was well within stipulated time frame as referred under UHSRC exempt review procedures. Further improvements may be possible in providing the detail package content to the PI by the office. In some of these cases the office provides the details of the missing or correct supporting documents after 1st review. These requirements of supporting documents may be provided to the PI well before he/she drafts the report in form of guideline document which might help in reducing the overall review time. The UHSRC Exempt Review Procedures have guidelines related to steps to submit the package, however it can be further extended towards the PI`s submission time limits as well. An expected time frame given to the PI may improve the PI's response timeline and thus efficiency towards overall time of the process.

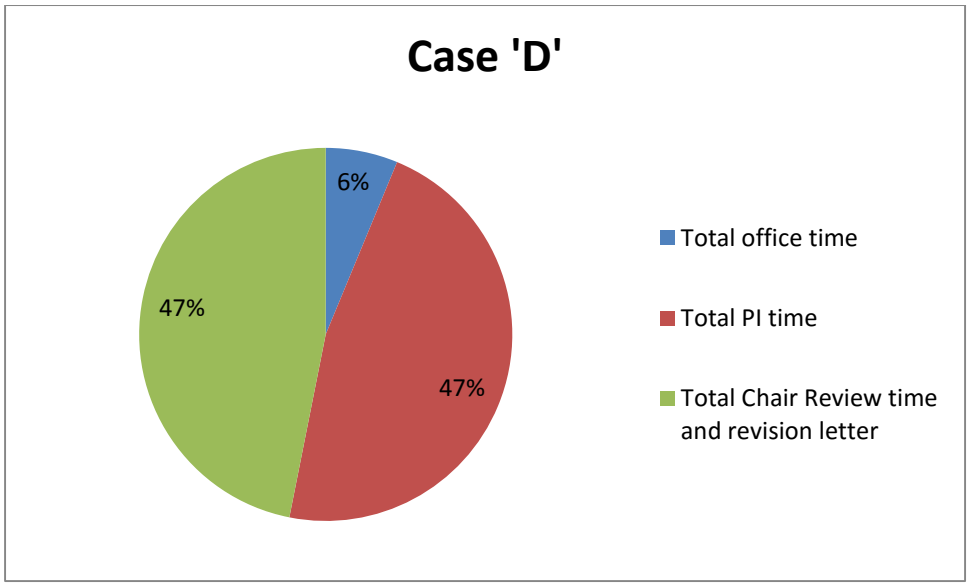
In addition if the pre-review process included an IRB Submission Application Checklist common to PI and office of UHSRC then the process completion time can be reduced and efficiency can be improved in the pre-review screening process. **(**IRB Develops Pre-review Screening Process, 2012**).** In one of the correspondence of the EMU Research Compliance Officer it was confirmed that similar checklist was used by the administrative office in the research review process at EMU as well, however towards the end of the process (S. Chawla, Personnel Communication, July 08, 2015). Use of such a checklist might increase the process efficiency especially if this checklist is used earlier in the process and by the principle investigator as well.

Principle Investigator's total time

The Principle Investigator's total time is the time taken to update the package and to respond to the revisions. Although the total time taken by the PI to revise the submission and to provide additional documents or respond to the reviewer comments varied greatly resulting in a SD of 5 (Table 1). In 50% of cases (case B, C, E, F, H, K, N and O) the PI responded on the same day; in cases F, H and K did not have any package errors or queries which resulted in a 0 days.

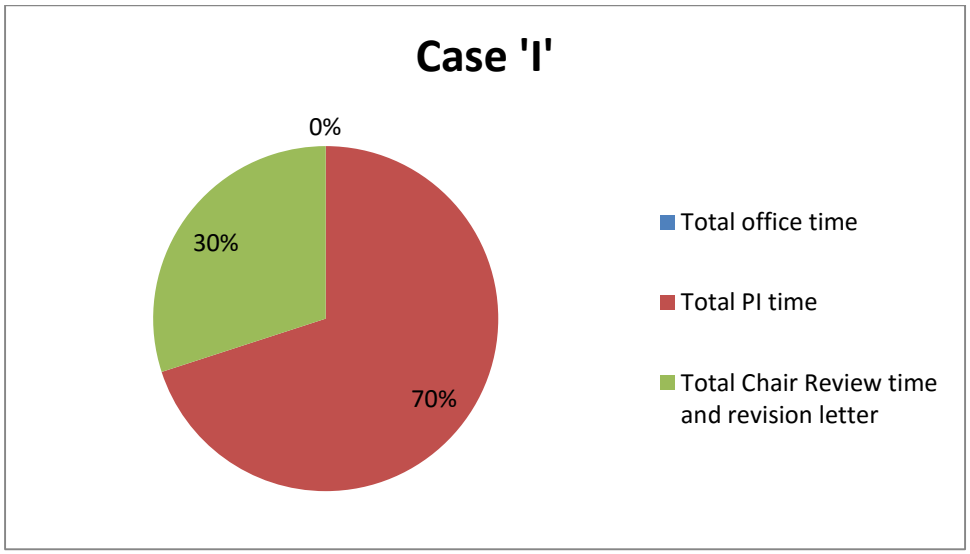
However, there were two cases where PI took 14-15 days to respond. In case D, the PI took a total of 15 days to respond (Figure 3). This was 47% of the total review process time. The package was unlocked twice by the office. The first update took the PI 5 days to respond; the second unlocked package took the PI 10 days to complete the revision.

Figure 3. **Case with maximum day turnover for PI time - Case D**



As of case I (Figure 4) the PI took 14 days to respond. Out of 14 days it took the PI 5 days to lock the package from the time the office unlocked it for the update and 9 days were taken to correspond back to the revision request done by the chair to him. In this case PI took 70% of the total time.

Figure 4. **Case with maximum day turnover for PI time - Case I**



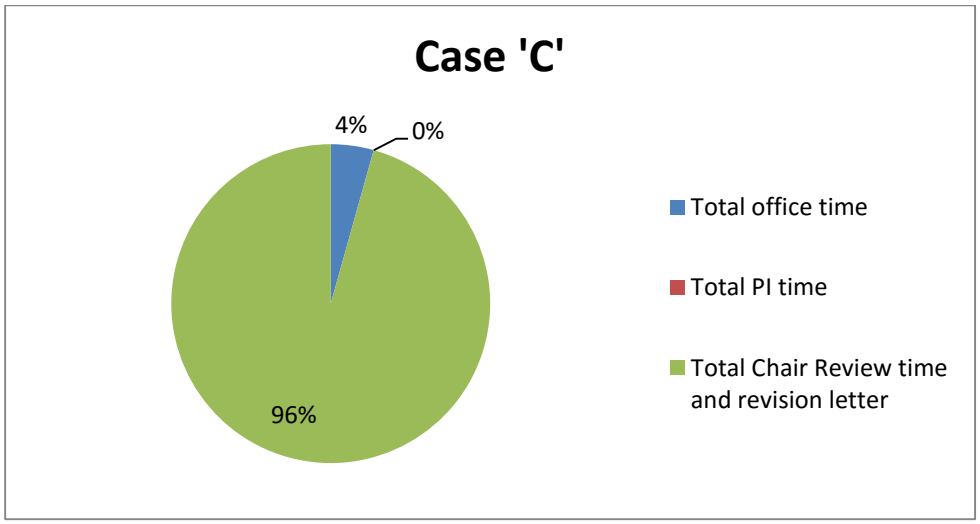
Chair reviewer's total time

Chair reviewers total time is the time taken to share the submission with other reviewers, review the submission and to send out final correspondence.

The average chair review time was 15 days and the max time taken by the reviewer was 22 days. These numbers do not truly represent the chair review time for 14 cases. For two cases G and H, the chair decided to send the submission to other reviewers and send the final correspondence of exempt or approval based on their decision. The Chair sent the final correspondence to the PI in less than 1 day for case G unlike case H where the chair took 3 days to send the correspondence. The SD of the chair review and correspondence was 7. The reason for the variation is clear. The minimum days taken by the chair were < 1 day as in case K. On the other hand the maximum review time taken by the chair was 22 days in case C (Figure 5). These 22 days consists of 16 days for review, 2 days for first correspondence and 4 days for final exempt letter correspondence.

The UHSRC exempt review procedures state that once the PI responds to the revision letter, the chair should correspond within 2 to 4 days. In these 14 cases, the minimum time taken by chair was <1 day and the max were 4 days.

Figure 5. **Case with maximum day turnover for chair response**



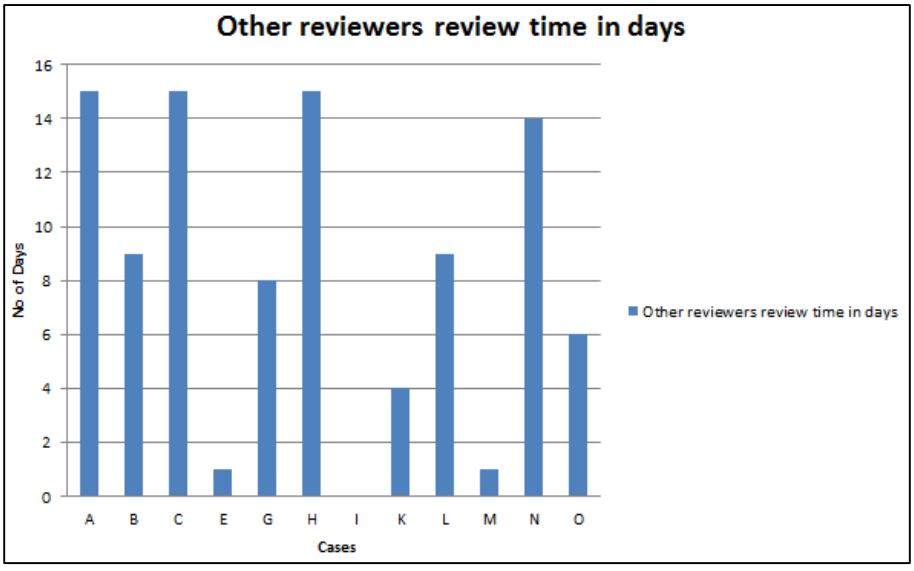
Note: Office took 4% time in this case and chair took 96% PI updated or responded on the same day of receipt

Other reviewer's time

The average time taken by other reviewers was 8 days with a min of 0 days (less than a day) and a max of 15 days.

There were 3 cases (case A, C and H) which crossed the 2 week or the 14 day criteria set in the UHSRC exempt review procedures. In terms of percentages, 21.42% of cases took extra time for review (Figure 6).

Figure 6. **Other reviewer's turnover time**



Mean/Average time taken by each group/party for all 14 cases

The average time taken to approve or exempt the cases was 15 days. Out of these 15 days 5% of this total time was taken by the office to review the package, and 20% of the time was taken by PI to update the package or respond to the chair. The remaining 75% of time was taken by chair to review and correspond with the PI.

The IRBNet database shows date and time of all the individual correspondence for every case. As each case has different category pertaining to the subject of research and the risk to conduct it, the individual stages takes various routes in correspondences as well as vary in review time. This may be presented in graphical form to indicate the current stage as well as time taken by these stages. The pictorial form of the data will help in understanding the bottleneck within the case and improve the time accordingly. A monthly report of the case to office may also help in understanding the efficiency of individual department.

Conclusion

The UHSRC exempt review process timelines displays that the EMU's Office of Research Compliance maintains good exempt review process when compared with the AAHRPP 2014 data and the UHSRC Exempt Review Procedures which display a median of 14 days and an average of 18 days review time, respectively.

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Appendix

Case	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
Status	Approved	Exempt	Exempt	Exempt	Exempt	Exempt	Exempt	Exempt	Exempt	Approved	Exempt	Exempt	Exempt	Exempt	Exempt
Submission notification	6-Mar-15	6-Mar-15	7-Mar-15	9-Mar-15	10-Mar-15	12-Mar-15	13-Mar-15	17-Mar-15	19-Mar-15	20-Mar-15	20-Mar-15	23-Mar-15	24-Mar-15	26-Mar-15	26-Mar-15
Package unlocked1	N/A	N/A	8-Mar-15	10-Mar-15	10-Mar-15	N/A	13-Mar-15	N/A	19-Mar-15	20-Mar-15	N/A	24-Mar-15	24-Mar-15	27-Mar-15	26-Mar-15
Office time 1	0	0	1	1	0	0	0	0	0	0	0	1	0	1	0
Revision complete1	N/A	N/A	8-Mar-15	15-Mar-15	10-Mar-15	N/A	16-Mar-15	N/A	24-Mar-15	20-Mar-15	N/A	24-Mar-15	24-Mar-15	27-Mar-15	26-Mar-15
PI time 1	0	0	0	5	0	0	3	0	5	0	0	0	0	0	0
Package unlocked2	N/A	N/A	N/A	16-Mar-15	N/A	N/A	N/A	N/A	N/A	20-Mar-15	N/A	N/A	N/A	N/A	N/A
office time 2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Revision complete 2	N/A	N/A	N/A	26-Mar-15	N/A	N/A	N/A	N/A	N/A	20-Mar-15	N/A	N/A	N/A	N/A	N/A
PI time 2	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0
Acknowledgement(sent to Chair)	8-Mar-15	8-Mar-15	8-Mar-15	26-Mar-15	10-Mar-15	12-Mar-15	16-Mar-15	17-Mar-15	24-Mar-15	20-Mar-15	20-Mar-15	24-Mar-15	25-Mar-15	27-Mar-15	26-Mar-15
Office time 3	2	2	0	0	0	0	0	0	0	0	0	0	1	0	0
Shared with reviewer	8-Mar-15	9-Mar-15	9-Mar-15	N/A	10-Mar-15	N/A	17-Mar-15	17-Mar-15	24-Mar-15	20-Mar-15	N/A	24-Mar-15	25-Mar-15	27-Mar-15	2-Apr-15
Chair time 1(share with reviewer)	0	1	1	0	0	0	1	0	0	0	0	0	0	0	7
Reviewer review complete	23-Mar-15	18-Mar-15	24-Mar-15	N/A	11-Mar-15	N/A	25-Mar-15	1-Apr-15	24-Mar-15	24-Mar-15	N/A	2-Apr-15	26-Mar-15	10-Apr-15	8-Apr-15
Reviewer time 1	15	9	15	0	1	0	8	15	0	4	0	9	1	14	6
Chair Review complete	23-Mar-15	18-Mar-15	24-Mar-15	10-Apr-15	24-Mar-15	24-Mar-15	N/A	N/A	24-Mar-15	25-Mar-15	20-Mar-15	2-Apr-15	26-Mar-15	10-Apr-15	8-Apr-15
Chair Review time 1	15	10	16	15	14	12	0	0	0	5	0	9	1	14	13
Package unlocked	24-Mar-15	18-Mar-15	26-Mar-15	N/A	N/A	N/A	N/A	N/A	30-Mar-15	24-Mar-15	N/A	2-Apr-15	28-Mar-15	N/A	13-Apr-15
Chair revision letter sent time 1	1	0	2	0	0	0	0	0	6	-1	0	0	2	0	5
Revision complete	25-Mar-15	18-Mar-15	26-Mar-15	N/A	N/A	N/A	N/A	N/A	8-Apr-15	25-Mar-15	N/A	6-Apr-15	29-Mar-15	N/A	13-Apr-15
PI time 3	1	0	0	0	0	0	0	0	9	1	0	4	1	0	0
Package unlocked	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	30-Mar-15	N/A	N/A
Chair Review time and /revision letter 2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Revision complete	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	30-Mar-15	N/A	N/A
PI time 4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Approve/Exp	25-Mar-15	18-Mar-15	30-Mar-15	10-Apr-15	24-Mar-15	24-Mar-15	25-Mar-15	4-Apr-15	8-Apr-15	25-Mar-15	20-Mar-15	6-Apr-15	30-Mar-15	10-Apr-15	13-Apr-15
Chair Review time and /revision letter 3	0	0	4	0	0	0	0	3	0	0	0	0	0	0	0