VOLUME I, ISSUE I

THE OFFICE OF
RESEARCH Newsletter

NEWTON-WELLESLEY HOSPITAL

nwh.org/research

Research at Newton-Wellesley

Message from the Office of Clinical Research

The Office of Clinical Research is excited and proud to re-introduce the Office of Research Newsletter after a brief sabbatical from publication.

The previous year was a busy time for the Office. We made significant changes and reaffirmed our commitment to responsible Human Subject Research.

After spending much of 2015 without a Manager to guide research activities, we hired a new Manager for the Office in early 2016 who immediately had to oversee the rigorous process for re-accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In March of 2016, we secured re-accreditation to remain a fully accredited institution with AAHRPP.

Since that time, we have hired a new Grants & Contracts Specialist to work with investigators to locate research

Continued on page 2

ISSUE I, SPRING 2017

CONTENTS

*Click story title, page number or picture to view Story

"Our Mission is to treat and care for all our patients and their families as we would a beloved family member"

New NIH Training Requirements for NIH-Funded Clinical Trials

In September 2016, NIH announced the requirement for all NIH-funded investigators and staff involved in the conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP). This new training requirement, **effective January 1, 2017**, applies to all new and existing NIH clinical trials. The policy requires basic GCP training and refresher courses every three years. The NIH policy can be found at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html.

To satisfy this new training requirement, all Newton-Wellesley Hospital investigators and study staff who are involved in an NIH-funded study meeting the NIH definition of a clinical trial will be required

Continued on page 2

Message from the Office of Research (continued)

funding opportunities, assist investigators with grant proposals, and with budget and contract negotiations for research activities.

In the past six months alone, we have worked with investigators to submit grant proposals for research funding in excess of $1.1 million and have already received approval for new projects totaling nearly $100,000.

As we await approval on the other grant proposals, we enter an exciting time at Newton-Wellesley and an exciting time for research in general. New rules, regulations, and guidelines governing Human Subject Research have been promulgated and approved.

A new White House Administration has taken shape and will further steer the direction of research through regulations and budgetary directives. In the local context, the Hospital has seen an increase in the number and type of studies evaluated for safety and feasibility to offer to patients.

This Issue of *The Office of Research Newsletter* will provide the research and hospital community with information about some of these local and national changes. It will highlight some of the novel studies and the investigators conducting those studies as well as provide general information about other research activities at Newton-Wellesley Hospital.

I wish to personally invite you to learn more about some of the

happenings and research at the Hospital by exploring the contents of this issue of the newsletter and our newly updated Office of Clinical Research website, nwh.org/research

Sincerely,

Office of Clinical Research

NIH Publishes new Good Clinical Practice Training Requirements (continued)

This [training] requirement applies even if research is conducted through a subcontract where the Prime is the direct recipient of NIH funding

to complete GCP training. This requirement applies even if the research conducted at Newton-Wellesley through a subcontract with the Prime Award recipient of the NIH funding for the clinical trial.

A clinical trial is defined by NIH as "a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes." See https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html.

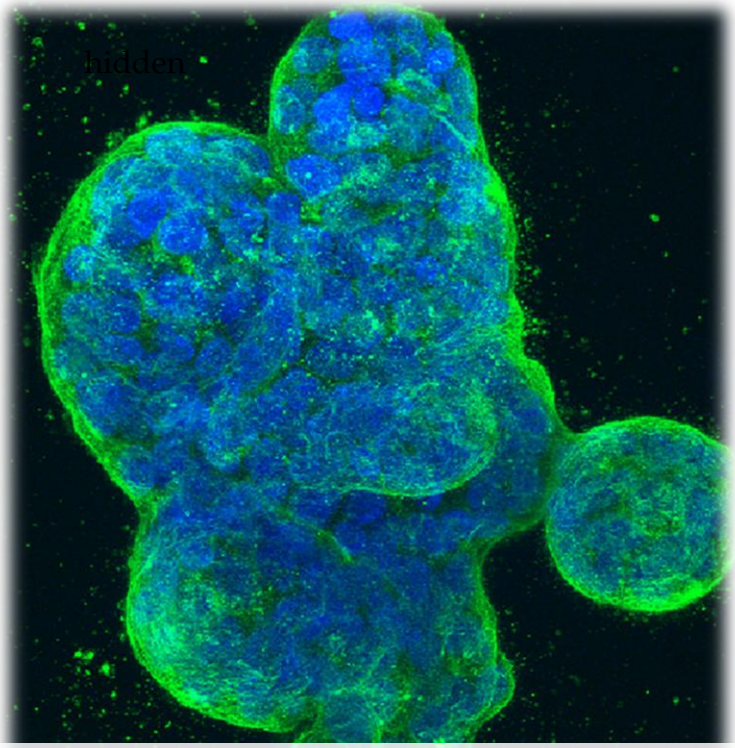
Investigators and staff will be required to complete the following GCP Course through CITI to satisfy this new training requirement:

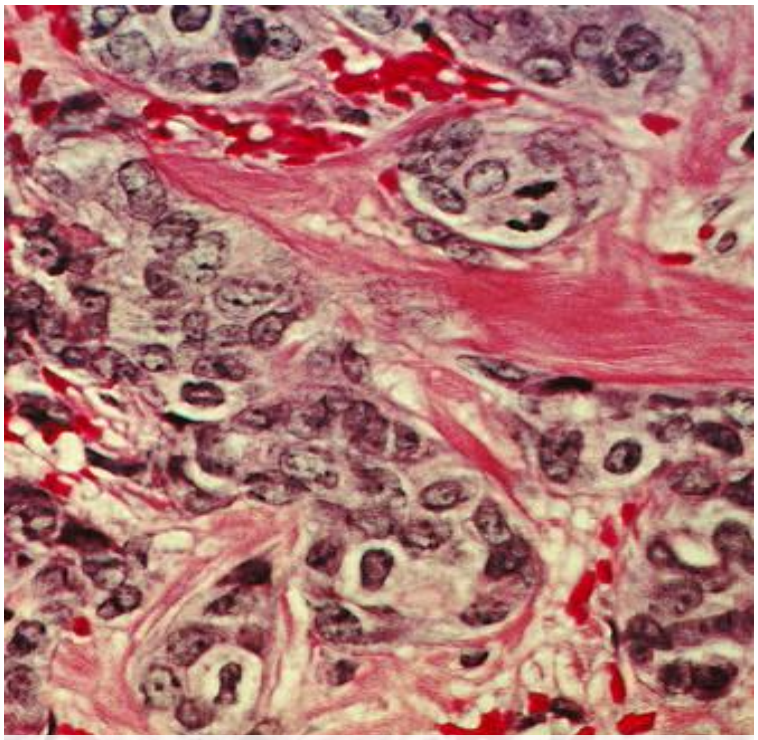
Photo provided by NIH Image Gallery

- GCP for Clinical Trials with Investigational Drugs and Biologics (ICH Focus)*

https://www.citiprogram.org/

For questions related to this new NIH-imposed training requirement please contact the Office of Clinical Research at 617-243-6493 or 617-243-6211.





Recently Opened Studies at Newton-Wellesley

Investigators at Newton-Wellesley Hospital are constantly opening innovative trials to provide patients with access to new treatments, therapies, and quality of life measures in both oncology and non-oncology fields. Investigators have recently opened the following featured studies, both of which are currently actively recruiting patients:

Oncology

Breast Cancer WEight Loss Study (BWEL Study)

Previous research has indicated that women that are overweight or obese at the time of initial diagnosis have a greater risk of their breast cancer recurring compared to women who were thinner at the time of initial diagnosis. The BWEL Study is a multi-site trial designed to evaluate whether overweight or obese women who participate in a weight loss program after an initial breast cancer diagnosis have a lower rate of cancer recurrence compared to those who do not participate in the weight loss program.

Amy Comander, MD, of the Vernon Cancer Center, is currently overseeing the BWEL Study here at Newton-Wellesley Hospital. Results from this study may help indicate whether weight loss programs should become a part of breast cancer treatment.

Individuals wishing to learn more about participation in the BWEL Study are encouraged to read additional information about the study here, or contact Dr. Comander.

Continued…

Left Photo depicts 3-Dimmensional culture of Breast cancer cells. Right Photo depicts histological slide of breast cancer tissue Photo(s) provided by NIH Image Gallery

Non-Oncology

ROADSTER 2 Registry Study

Carotid Artery Disease is a serious condition where plaque can build up in the carotid arteries, leading to a decrease in blood flow to the brain or even blood clots. This decrease in blood flow or migration of plaque or blood clots to the brain could ultimately result in a stroke.

Newton-Wellesley recently opened the ROADSTER 2 Registry Study to evaluate real world usage of the ENROUTE Transcarotid Stent when used by physicians in combination with the ENROUTE Transcarotid Neuroprotection System in the treatment of narrowing of the carotid artery with a stent procedure. Opening this study at Newton-Wellesley affords our patients the same opportunity to participate as might normally be available at larger research hospitals with the same access to highly experienced physicians.

Both the ENROUTE Transcarotid Stent and the Transcarotid Neuroprotection System are FDA approved devices that may be used in research studies and patient care. Several of these procedures have now been successfully performed at Newton-Wellesley Hospital by Christopher Kwolek, M.D., Chair of Surgery and Chief of Vascular Surgery.

For information about eligibility to participate in the ROADSTER 2 Registry, click here or contact Dr. Kwolek.

NIH Moves to Advance Collaborative Research on a National Scale with SMART-IRB

The NIH Policy on the Use of a Single Institutional Review Board (sIRB) of Record for Multi-Site Research establishes the expectation that all sites participating in multi-site studies involving non-exempt human subject research funded by the National Institutes of Health (NIH) will use an sIRB to conduct the ethical review required by the Department of Health and Human Services.

Continued…

ANNOUNCEMENTS

RESEARCH GRAND ROUNDS

Hospital Community Members are invited to attend the annual Research Grand Rounds on **June 7, 2017** from **7:30 – 9:30 am** in the **Shipley Auditorium**

Podium Presentations begin promptly at **8:00 am** after a continental breakfast

Presenters will be the **Top 3 Abstract Submissions** from the Call for Abstracts Competition

For additional information, contact the Office of Research

FUNDING OPPORTUNITIES

FEDERAL

AACN – IMPACT RESEARCH GRANT

AMERICAN CANCER SOCIETY

PCORI

LOT PAGE INTERNAL AWARDS

(Continued)

What is SMART IRB?

SMART IRB (Streamlined, Multisite, Accelerated Resources for Trials Institutional Review Board) was developed under an NIH grant and is a platform designed to ease common challenges and burdens associated with initiating multi-site research. SMART IRB will eliminate duplicative IRB reviews while maintaining appropriate oversight.

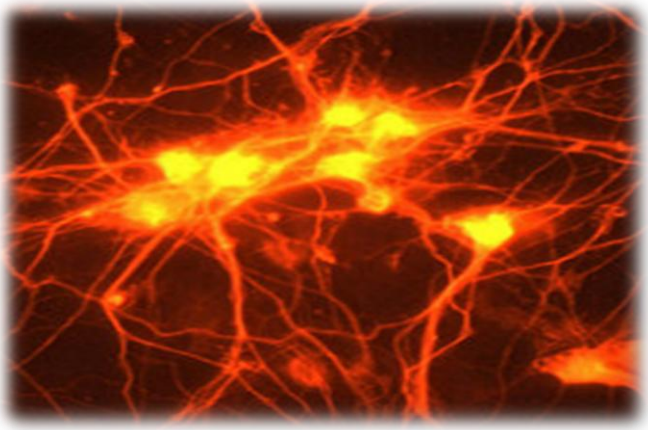
The NCATS SMART IRB Reliance Platform provides a harmonized approach, so that the platform can easily be used by any clinical research network or even a single investigator wishing to conduct a multisite clinical study. The platform can be used for a range of studies, from large complex clinical trials to two-site collaborations. Clinical investigators will be able to obtain trial results faster and, ultimately, speed development of new diagnostics, treatments and preventative measures for patients.

SMART IRB will support and encourage nation-wide collaboration through a flexible master IRB reliance agreement, standard operating procedures and complementary tools and resources.

It is also designed to provide a roadmap to implement the National Institutes of Health (NIH) Policy on the Use of Single Institutional Review Board for Multi-Site Research.

Newton-Wellesley Hospital recently joined over 125 other institutions choosing to use the SMART IRB for participation in NIH funded multisite clinical research studies.

For additional information on the SMART IRB, visit the Newton-Wellesley Hospital SMART IRB webpage.



Featured Study and Investigator: MCT Oils with David Berkowitz. Photo shows sprouting connections in the brain between brain cells. Photo provided by NIH Image Gallery

Featured Study and Investigator: MCT Oils with David Berkowitz

Research leads to new medical discoveries every day. These discoveries have led to an increased life-span for many Americans. The US Census Bureau estimates that by the year 2030, there will be nearly 83.4 million Americans living in the US above the age of 65.

Naturally, this means that more and more Americans will need medical care later in life. Older patients are often times treated and hospitalized for an extended timeframe which may give rise to the development of secondary afflictions. As the population continues to age, these problems are only likely to continue to develop unless remedial and preventative steps are taken.

Newton-Wellesley's David Berkowitz, Assistant Director of Clinical Pharmacy, initiated a new pilot study last October to test the effects of Medium Chain Triglycerides (MCT) on the development of delirium in older hospitalized patients. The Research Office recently sat down with him to discuss his study.

Continued...

(Continued)

About the Study

Office of Clinical Research: Tell us a little about this study.

David Berkowitz: We are studying ways to decrease the incidence of a condition called Hospital-acquired delirium. Hospital-acquired delirium is a medical condition that can happen when someone is sick and in a new environment – It causes confusion and disorientation, and can include delusions and agitation which can be upsetting for the patients and their families and can negatively impact the patient's health.

OCR: This sounds like an important issue that needs investigation.

DB: [This condition] can affect up to 20% of high risk patients during their admission. There currently aren't any good ways to prevent hospital-acquired delirium, and no medications have been shown to reduce the length of delirium. One of the main risk factors for delirium is older age, and generally speaking our patient demographic [at the Hospital] tends to be on the older side. Thus, this is a common disorder here.

OCR: What do you hope to discover from this study?

DB: Our hypothesis is that delirium is partially attributed to an alteration in glucose oxidation in the brain. We are hoping to overcome that derangement by using an alternative source of energy in the form of Ketones which are a byproduct of MCT Oil metabolism. Once the study is complete, we hope to submit for publication – however because it is a pilot study, we will not meet the statistical significance based on the number of subjects. Hopefully this pilot study will generate broad interest in conducting a randomized control trial.

OCR: Have you encountered any challenges with this pilot study?

DB: So far our main challenge has been recruiting patients.

OCR: Unfortunately, your study is not unique with that specific challenge. What made you look into this condition?

DB: This study is important to me because both my grandfather and wife's grandfather suffered from hospital-acquired delirium prior to passing away, so I have firsthand experience with how frightening this can be for families.

OCR: I hope you can get the results you need to further investigate this condition that is obviously very important to you. What are some other research areas that are important to you?

DB: My general research interests include population health, antimicrobial stewardship, direct oral anticoagulants, medications which are associated with falls, medication adherence and related devices, expiration dating and hospital waste, medication safety, and interoperability of [Electronic Health Record's] using block chain technology.

OCR: That sounds like a lot of research interests. Do you have any projects planned or in development to test any of those interests?

DB: I have two current projects in the planning phase. The first is to study a medication adherence device for direct oral anticoagulants and the second is a project to set up a multi-healthsystem registry for allergy information using block chain.

OCR: Those sound very cutting-edge. Have you been at the forefront on other novel studies in the past?

DB: The MCT Oil Study is my first IRB-approved research study. I have done a few QI (Quality Improvement) projects in the past – most notably to increase patient access to intranasal naloxone.

OCR: It may be your first IRB-approved study, but it does not sound like it will not be your last. Thank you for taking a few moments to speak with us about your study and research interests.

Continued...

About the Investigator

David Berkowitz is the Assistant Director of Clinical Pharmacy at Newton-Wellesley Hospital. He received a bachelor's and doctorate degree in Pharmacy (PharmD) from the Massachusetts College of Pharmacy in Boston, MA. He has worked at Newton-Wellesley Hospital since 2014. David is a 2015 Partners in Excellence Award for Healthcare Innovation recipient and part of the 2015 Partner's Pharmacy and Therapeutics Partner's in Excellence Team Award.

More Information:

This study is being conducted under the oversight, supervision, and approval of the Newton-Wellesley Hospital Institutional Review Board

David Berkowitz does not work for, consult for, own shares in, or otherwise receive funding or monetary honorarium from any company that may benefit from this article and has no relevant affiliations beyond his appointment to Newton-Wellesley Hospital.

Lot Page Internal Awards Funding Opportunity

The Lot Page Research Fund is an internal peer reviewed research award program designed to expand and foster research activities at the Hospital. Submissions are open to all applicants that have a primary clinical appointment at Newton-Wellesley Hospital.

The funding opportunity is for an 18-month grant of up to $20,000 and investigators are limited to receiving one award per fiscal year.

Proposals are reviewed for funding under two separate funding cycles. The Spring Cycle awards funding for the project period that runs from April 1 to September 30, with applications due by March 1 – The Fall Cycle awards funding for the project period that runs from November 1 to April 30 with applications due by September 1.

The application and awarding process for the Lot Page Research Fund has recently received an update to provide for increased opportunities and accountability. Among the changes are a new application which can be downloaded from the Internal Awards and Research Grand Rounds webpage and a new notice of awards agreement that provides for interim and final reporting on the grant.

Additional information on the Lot Page Research Fund is available on the Office of Clinical Research website. Questions can be submitted to the Office here.

Final Rule Aims to Enhance Protections for Research Participants and Modernize Regulatory Oversight

The U.S. Department of Health and Human Services recently issued a final rule to update the "Common Rule" regulations (45CFR46) that provide protections for individuals who participate in research. The current regulations have been in place since 1991. When they were developed, research was conducted predominantly at universities and medical institutions, and each study generally took place at a single site. Since then, research with human participants has grown in scale and complexity, become more diverse, and data has entered the digital age.

Most provisions in the new rule will go into effect in 2018.

Besides strengthening protections for people who volunteer to participate in research, the new rule also ensures that the oversight system does not add inappropriate administrative burdens, particularly with respect to research that is considered low risk. The update also allows more flexibility in responding to today's rapidly evolving and dynamic research environment.

Among the more significant changes is that the final rule will now generally expect consent forms to include a concise explanation – at the beginning of the document – of the key information that would be most important to individuals contemplating participation in a particular study. This will enable potential participants to have a better understanding of a project's scope, including its risks and benefits, in order to make a more fully informed decision about whether to participate.

"Over the years, many have argued that consent forms have become these incredibly lengthy and complex documents that are designed to protect institutions from lawsuits, rather than providing potential research subjects with the information they need in order to make an informed choice about whether to participate in a research study," said Jerry Menikoff, MD, Director of HHS Office for Human Research Protections. This led to the government's recent efforts to overhaul the regulations.

Other key elements in the final rule include:

- Requirements to use a single institutional review board (IRB) for multi-institutional research studies. Flexibility has been incorporated to allow for broad groups of studies (instead of just specific studies) to be removed from this requirement.

- For studies involving stored identifiable data or identifiable biospecimens, researchers will have the option of relying on broad consent obtained for future research as an alternative to seeking IRB approval to waive the consent requirement. Researchers will still not have to obtain consent for studies on non-identified stored data or biospecimens

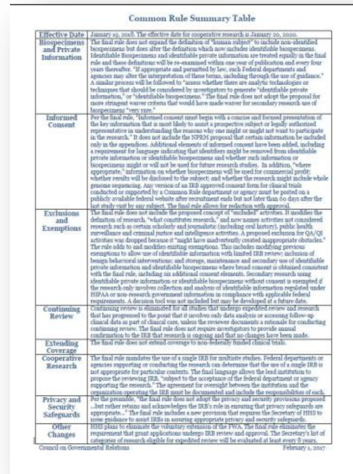
- The establishment of new exempt categories of research based on the level of risk they pose to participants. For example, to reduce unnecessary regulatory burden and allow IRBs to focus their attention on higher risk studies, there is a new exemption for secondary research involving identifiable private information if the research is regulated by and participants are protected under the HIPAA rules.

Continued...

Final Rule (continued)

- Removal of the requirement to conduct continuing review of ongoing research studies in certain instances where such review does little to protect subjects.
- Requirement that consent forms for certain federally funded clinical trials be posted on a public website.

For a simplified look at some of the changes, please consult the summary table to the right created by the Council On Government Relations.



Common Rule Summary Table

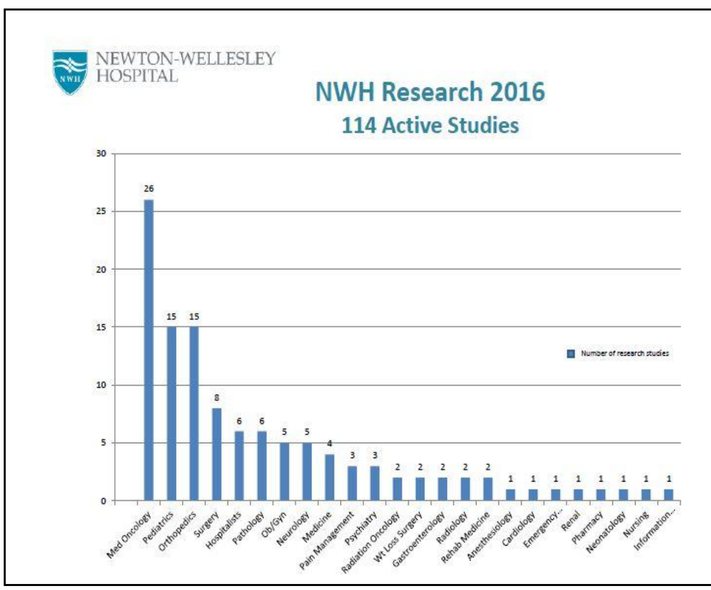
Effective Date	January 19, 2018. The effective date for cooperative research is January 20, 2020.
Biospecimens and Private Information	The final rule does not expand the definition of "human subject" to include non-identified biospecimens but does alter the definition which now includes identifiable biospecimens. Identifiable Biospecimens and identifiable private information are treated equally in the final rule and these definitions will be re-examined within one year of publication and every four years thereafter. "If appropriate and permitted by law, such Federal departments and agencies may alter the interpretation of these terms, including through the use of guidance." A similar process will be followed to "assess whether there are analytic technologies or techniques that should be considered by investigators to generate "identifiable private information," or "identifiable biospecimens." The final rule does not adopt the proposal for more stringent waiver criteria that would have made waiver for secondary research use of biospecimens "very rare."
Informed Consent	Per the final rule, "Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research." It does not include the NPRM proposal that certain information be included only in the appendices. Additional elements of informed consent have been added, including a requirement for language indicating that identifiers might be removed from identifiable private information or identifiable biospecimens and whether such information or biospecimens might or will not be used for future research studies. In addition, "where appropriate," information on whether biospecimens will be used for commercial profit; whether results will be disclosed to the subject; and whether the research might include whole genome sequencing. Any version of an IRB approved consent form for clinical trials conducted or supported by a Common Rule department or agency must be posted on a publicly available federal website after recruitment ends but not later than 60 days after the last study visit by any subject. The final rule allows for redaction with approval.
Exclusions and Exemptions	The final rule does not include the proposed concept of "excluded" activities. It modifies the definition of research, "what constitutes research," and now names activities not considered research such as certain scholarly and journalistic (including oral history), public health surveillance and criminal justice and intelligence activities. A proposed exclusion for QA/QI activities was dropped because it "might have inadvertently created inappropriate obstacles." The rule adds to and modifies existing exemptions. This includes modifying previous exemptions to allow use of identifiable information with limited IRB review; inclusion of benign behavioral interventions; and storage, maintenance and secondary use of identifiable private information and identifiable biospecimens where broad consent is obtained consistent with the final rule, including six additional consent elements. Secondary research using identifiable private information or identifiable biospecimens without consent is exempted if the research only involves collection and analysis of identifiable information regulated under HIPAA or non-research government information in compliance with applicable federal requirements. A decision tool was not included but may be developed at a future date.
Continuing Review	Continuing review is eliminated for all studies that undergo expedited review and research that has progressed to the point that it involves only data analysis or accessing follow-up clinical data as part of clinical care, unless the reviewer documents a rationale for conducting continuing review. The final rule does not require investigators to provide annual confirmation to the IRB that research is ongoing and that no changes have been made.
Extending Coverage	The final rule does not extend coverage to non-federally funded clinical trials.
Cooperative Research	The final rule mandates the use of a single IRB for multisite studies. Federal departments or agencies supporting or conducting the research can determine that the use of a single IRB is not appropriate for particular contexts. The final language allows the lead institution to propose the reviewing IRB, "subject to the acceptance of the federal department or agency supporting the research." The agreement for oversight between the institution and the organization operating the IRB must be documented and include the responsibilities of each.
Privacy and Security Safeguards	Per the preamble, "the final rule does not adopt the privacy and security provisions proposed ...but rather retains and acknowledges the IRB's role in ensuring that privacy safeguards are appropriate..." The final rule includes a new provision that requires the Secretary of HHS to issue guidance to assist IRBs in assuring appropriate privacy and security safeguards.
Other Changes	HHS plans to eliminate the voluntary extension of the FWA. The final rule eliminates the requirement that grant applications undergo IRB review and approval. The Secretary's list of categories of research eligible for expedited review will be evaluated at least every 8 years.

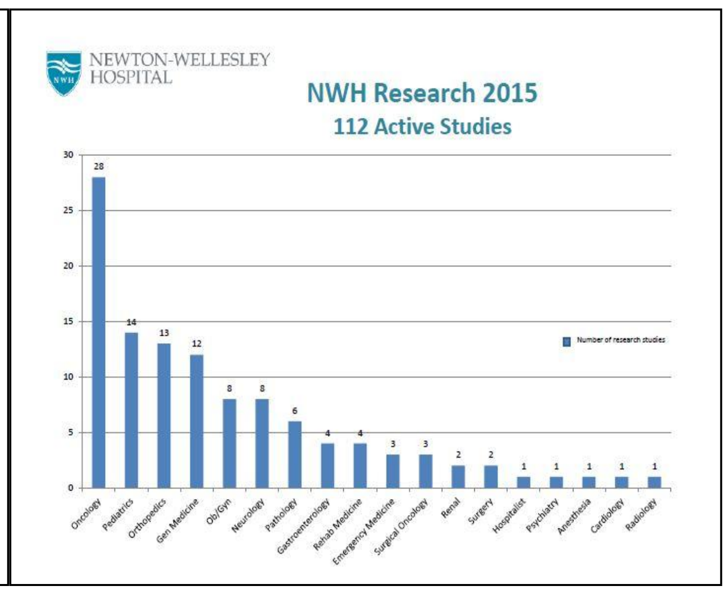
Council on Governmental Relations February 1, 2017

Summary Table created by COGR

Click on Table for an expanded view.

Research Study Activity at Newton-Wellesley





Click Left (2016) chart to expand view. To return to standard view, click Right (2015) chart.

The total number of active research studies in progress at Newton-Wellesley Hospital for 2016 was 114, which represents a minimal increase of 2 protocols over the previous year. While we saw only the slightest increase in the number of active studies, more departments have become engaged in research over the past year to include pharmacy and nursing. Similar to prior years, Oncology studies again represented approximately 25% of the trials in 2016, with a total of 26 active studies.

Continued...

Newton- Wellesley had 12 industry-sponsored studies active in 2016. Total available research funds at the end of 2016 were $359,233.37, which reflects a 60% increase in sponsored projects over 2015. This next year, we expect continued expansion in our research portfolio and collaborations.

The Office of Research Newsletter is the electronic newsletter produced and distributed by the Newton-Wellesley Hospital Office of Clinical Research to highlight important and current news in the field of research.

Questions or Comments regarding *The Office of Research Newsletter* should be directed to the Office of Clinical Research

If you have a news story or research activity that you would like to highlight in the next issue, please contact the Office of Clinical Research to discuss

THE OFFICE OF
RESEARCH Newsletter
NEWTON-WELLESLEY HOSPITAL
nwh.org/research

2014 Washington Street
Newton, MA 02462

[Recipient]

Address Line 1
Address Line 2
Address Line 3
Address Line 4