Policy on Patient Privacy and Clinical Data Protection
CLEAR-III / MISTIE / ICES Clinical Trials

BIOS is committed to respecting the privacy of patients participating in our sponsored clinical trials and to ensuring that patient data is used responsibly and in compliance with internationally recognized standards of privacy protection. These standards include but are not limited to the European Union Data Protection Directive (95/46/EC) and its associated Safe Harbor principles, privacy rules (45 CFR Part 160, 164) of the U.S. Health Insurance Portability and Accountability Act (HIPAA), the U.S. Food & Drug Administration (FDA) clinical trial regulations as well as similar international Good Clinical Practice standards (GCPs), and U.S. Department of Health & Human Services (DHHS), U.S. National Institute of Health (NIH), and FDA codifications of federal policy for the protection of human subjects (Common Rule).

Definitions and Background

For the purposes of this document, “Protected Health Information” (PHI) encompasses the regulatory definitions of “personal data” and “personal information” as described in European Directive 95/46/EC in regards to the transfer of individually identifiable health information to the U.S., as well as “Protected Health Information” as defined in the HIPAA regulations. The term “subject” refers to a medical patient at any of the participating clinical trial sites who has enrolled, or will be enrolled, in one of the above-listed clinical trials.

Generally speaking, PHI is any information that could potentially be used, alone or in combination, to identify a patient, even if it would require having access to restricted-access data repositories such as the hospital’s medical records system. The list of potential “identifiers” is very broad. It includes the patient’s name, any unique identifying numbers (example: social security number, medical record number, driver’s license number), any geographic location information smaller than a state (example: street, city, county, zip code), any electronic identifiers traceable to the subject (example: telephone number, email address, web page URLs, computer IP address), biometric and visual identifiers (example: recognizable photos or videos, fingerprints, voice recordings) and all elements of dates directly related to the individual (examples: birth date, admission or discharge date, date of death, any procedure or medical event date & time that could be traced back to that patient through the medical chart or hospital records). Additionally, for the relatively smaller group of patients over age 89 years, the patient’s age and the year of birth are also considered to be PHI.
Policy and Basic Principals

In keeping with our patient privacy commitments, BIOS has enacted this policy, implemented certain internal procedures, and obtained contractual commitments intended to enforce the following basic principles.

Notice & Choice

No personally-identifiable data will be collected without first making notice to the subject that voluntary participation in one of the above listed BIOS-sponsored clinical trials will entail review and collection of PHI. In keeping with GCP standards, the patient must grant proper Informed Consent before any data is collected for the study. As part of the informed consent process, the potential subject should be given the choice to refuse participation in the clinical trial on the grounds of privacy (and in accord with GCP standards, for any other reason whatsoever). The subject’s decision to participate should be documented both in the medical chart and by way of a written, properly-executed informed consent (for U.S. sites, a separate HIPAA consent may also be used per IRB requirements) that fully complies with all applicable European Directive, GCP and Common Rule regulations, as well as local IRB/EC and participating clinical site requirements. The only exception is the situation where an IRB/EC at a clinical site has granted a waiver of the informed consent requirements allowing collection of PHI involving no more than minimal risk to the subject’s privacy for a specific limited purpose (such as preliminary patient screening) in the case where the clinical trial could not practicably be conducted without access to and use of the PHI.

Purpose

Clinical trial data will be used only for the purposes stated in the informed consent to support the conduct of the clinical trial, or as may be required by applicable regulations that govern clinical trials (such as for the purpose of review by a regulatory agency audit), and not for any other purpose. Only the data necessary for the trial to evaluate the safety and efficacy of the test article, to monitor the safety of the patients in the trial, and to ensure compliance with the requirements of the study protocol and the applicable GCP regulations shall be collected.

Restricted and Limited Disclosure

Data will not be further disclosed without the subject’s consent. All organizations that will have access to the PHI should be expressly listed in the Informed Consent

Security

Data will be kept secure from any potential abuses. Access to the data will be controlled.
Data Processing

All processing of personal data is, by consent, for the purposes listed above and under the control of the data controller. Individuals have the right to:

- Obtain copies of their data
- Correct their data
- Prevent processing for direct marketing
- Withdraw consent to processing with its consequential effects
- Prevent non-core purpose disclosures
- Prevent trans-border disclosures to third parties where there are inadequate data protection arrangements.

BIOS shall comply with internationally recognized standards that require the processing of personal data, both automated and manual, and meet the following data protection principles:

- Data has fair and lawful processing
- Data is obtained only for specified and lawful purposes and is not processed in any incompatible manner
- Data use is adequate and relevant but not excessive
- Data is kept current (where necessary) and accurate
- Data is not kept longer than necessary
- Data processing is in accordance with the rights of data subjects
- Data is protected by appropriate security measures
- Data is not transferred to third parties unless an adequate level of data protection exists

Data Collection

Every effort is made to ensure that the information is accurate and up-to-date and all communications with patients provide easy means of validating, correcting errors and updating information.

Data Security

BIOS maintains a high level of security in relation to data. Computer equipment, networks, programs, data and documentation are maintained to a high standard, and access to data and equipment is at all times restricted to appropriate staff.

The handling of medical information obtained in clinical research is governed by national and international data protection regulations and medical confidentiality. Any medical information collected will be maintained under these regulations.

Release, Sharing or Transference of Data

The information provided to us will be available to BIOS and authorized organizations and individuals working as agents of BIOS in support of the conduct of our clinical trials. Access to data and equipment is at all times restricted to appropriate staff. BIOS will not trade, sell,
release, share or transfer any personal information for use by any business outside the list of organizations listed in the informed consent without the subject’s consent, or in a form other than what was disclosed at the time the information was collected, unless permitted or required by law.

Under some circumstances BIOS may be required by law enforcement or judicial authorities to provide personal information as required by law to the appropriate government authorities.

Companies working as agents of BIOS are required to sign confidentiality agreements and provide assurance agreeing to handle all confidential information containing personal data in accordance with applicable law, including but not limited to, the European Data Protection Directive [EC/95/46] and the HIPAA privacy rule.

BIOS may transfer patient data to one of its databases outside the patient’s country of domicile.

Overview of Privacy-Related Procedures and Practices

To enforce this policy, BIOS implements certain standard procedures and practices as well as obtains legal commitments from its employees and agents related to data privacy and security.

Clinical sites participating in our clinical trials should take reasonable steps to remove or obscure as many of the PHI identifiers as possible, especially direct identifiers such as the patients name and medical record number, from any documents or electronic records that are provided to the clinical trial team (such as copies of procedure reports and “source documents”). Likewise, the paper-based or electronic data capture records (“case forms” or EDC web forms) shall not collect such basic patient identifiers. Financial documents such as billing and insurance information should never be released to the study team (albeit they might be inadvertently eyes-only viewable during an on-site monitoring visit).

Notwithstanding these reasonable attempts to “blind” the patient’s identity, our clinical trials, like most others, require certain timing information such as the date and time of various clinical tests, assessments, and medical events in order to determine the sequence of study events. Also for covariate analysis purposes, it is necessary to capture certain demographic data (for example: age, sex, gender, ethnicity, medical history, concomitant medications, research facility) as well. Although the patient will only be identified and referenced in the case report forms and within the clinical database by way of a masked subject code (site & patient number), for the reasons noted, it is not possible to completely eliminate all potential PHI identifiers in collected source documents and procedure reports. Participating clinical trial sites are expected to note this fact in their respective informed consent documents.

Furthermore, for the purposes of monitoring the clinical trial to ensure the validity and completeness of the clinical data as well as the compliance of the clinical sites with GCP regulations and the requirements of the study protocol, it is necessary for certain BIOS staff to have access to the full, un-obscured patient medical record, which necessarily will include identifiers such as the patients name and medical record number as are required to match the clinical data to the patient’s medical records and to confirm the
subject’s legitimacy. This requirement for access to and review of the patient medical records is described in European clinical trials directive (2001/20/EC) and the European data protective directive (95/46/EEC) as well as Good Clinical Practice standards. BIOS practices are in full compliance with these directives and standards.

BIOS uses a web-based Electronic Data Capture (EDC) system both for compiling & processing clinical data and to facilitate the monitoring and source document verification processes. Our clinical sites are required to scan and upload certain patient medical records to this restricted-access regulatory-compliant EDC system. This includes “bedside worksheets” & various study data collection forms, procedure reports, progress & nursing notes, lab reports, admit/discharge reports, consultations, patient questionnaires, facility transfer and emergency transport records, medical histories, medication records, ER records, ICU flow sheets, death & autopsy reports, adverse event reports, and similar medical records. Notably, it also includes DICOM-formatted electronic files and images from radiology procedures, as well, in the case of some clinical trials, video and audio recordings of patient interviews that potentially include a recognizable patient image and voice, possibly also including family members that might be in the room at the time (provided they have granted a separate consent to be videotaped). Access to these uploaded patient records and data/video files is strictly limited to only those staff involved in the monitoring, quality assurance and safety review of these documents. This includes the monitoring staff (for assigned sites only), the safety officer, the ICH and surgical medical monitors, the safety/efficacy endpoint committee members, the surgical reviewers, and the site and overall project management staff, including the sponsoring investigator. Videos, specifically, are only assessable to, and reviewed by, a special outcomes committee, and then only after any mention of the patient’s name or other directly-identifying information has been removed from the recording. Of course, the investigational site staff members (investigator and authorized facility staff) have access to their patient’s records, but not to any other subjects.

As discussed above, the sheer volume and number of uploaded records, as well as the need for certain identifiers to confirm the documents have been uploaded to the proper subject, makes blinding all PHI identifiers impossible. For that reason, access to the EDC system is highly restricted to only specific members of the study team. The EDC system has predefined “roles” that control each user’s access to the clinical data and uploaded study documentation, on a field-level basis. As discussed below, the granting of access to the EDC system and the assignment of access roles is strictly controlled. Similarly, the EDC system restricts access on both a by-study and by-site level, meaning that only staff members that are assigned to a specific investigational site (hospital) are able to view the clinical data and uploaded medical records (PHI) from subjects at that investigational site.

In accordance with BIOS standard operating procedures and as enforced via the EDC system’s built-in role restrictions, only the “Project Coordinator” (PC) role and, as a backup when the PC is unavailable, the “Project Manager” role may grant anyone access to the EDC system. These roles are held by the BIOS Data Manager and the Monitoring/Quality Assurance Manager respectively. When a new user requests access to the EDC system, the Project Coordinator must first confirm that the requestor is an authorized member of the study team. This is done by confirming the requestor is identified and authorized within the investigational site documentation, including the investigator’s Delegation of
Responsibility form and the IRB/EC’s listing of authorized clinical site staff as well as other credentials such as curricula vitae and other study-mandated regulatory documentation. Next, the identity of the requestor must be verified. This is accomplished by requiring the individual to make the request via an identifiable private email address assigned by the hospital (example: recognizable_name@participating_hospital.edu); access will not be granted to users with public email addresses (Google, Yahoo, etc.).

Also, before the user may obtain access to the EDC, he or she must complete an online course, including passing a test, covering the proper use of the system and the importance of maintaining the security of the EDC system. Each user also must sign a written document, in accordance with HIPAA, FDA 21-CFR-11, and similar regulations, verifying their acknowledgement that the EDC system potentially contains PHI for which they are legally bound (both civil and legal liability) to protect. Passwords within the system must be changed immediately upon first log-in and again at 90-day intervals. The system will automatically log-out the user after 30 minutes of inactivity. Additionally, this “EDC Electronic Signature and PHI Confidentiality Agreement” requires individuals to take certain other precautions (locking screen savers, shredding of any print-outs, complex, “non-guess-able” passwords, etc.) designed to enhance the security of the system.

Design and development of the EDC system was made in accordance with the FDA Guidance for Industry on Computerized Systems Used in Clinical Trials (April 1999) as well as the Electronic Records/Electronic Signatures rule (21 CFR part 11). A secure, computer generated, time-stamped electronic audit trail allows reconstruction of the course of events relating to the creation, modification, and deletion of any electronic record within the system; all user actions within the system are attributable and traceable. All data are electronically signed by the originator and by the monitor/reviewer via a legally-binding electronic equivalent of the individual's handwritten signature. Data and uploaded files/documents within the EDC system are stored on computer servers maintained in a physically secured, guarded data center operating under strong security measures. Collected data and medical records are retained in accordance with applicable regulations regarding the retention of clinical trial data.

As discussed herein, BIOS’s privacy and security measures are extensive, probably more so than traditional clinical trials employing paper case report forms and on-site monitoring visits. Traditionally, clinical research associates visit sites at frequent intervals and collect paper copies of various study documents. These are then personally transported (or sometime faxed or shipped via courier) back to the sponsor for storage. Such outdated methods entail the significant risk that paper documents can be inadvertently released. In sharp contrast, BIOS uses its EDC system instead for the collection of “source documents” and patient data. Uploading and retention within the system is far more secure in comparison. No paper documents are stored, either at the sponsor or in unsecured locations at the clinical sites.

In summary, BIOS is committed to, and is fully-compliant with, international privacy standards.
APPENDIX 1: Organizations Having Access to Patient Data & Medical Records

Authorized staff at the following organizations have roles allowing the ability to review patient documentation, including uploaded medical records.

- Johns Hopkins University (Regulatory Sponsor & Trial Coordinating Center)
- University of Chicago (Surgical Center for CLEAR-III)
- University of Cincinnati (Surgical Center for MISTIE)
- University of California, Los Angeles (Surgical Center for ICES)
- University of Glasgow (Outcomes Coordinating Center, Video Review & Adjudication)
- Wayne State University (MISTIE Pharmacokinetic Data)
- Boston University (Medical Event Monitoring)
- Emissary International LLC (Contract Research Organization)
- Cohen Associates (Contract Research Organization)

APPENDIX 2: Sample Informed Consent Language

CLEAR-III:

Study information collected about you will be given to the sponsor.

For regulatory purposes, the sponsor of this trial is Dr. Daniel F. Hanley, a neurologist and the director of the Brain Injury Outcomes Program at the Johns Hopkins University School of Medicine in Baltimore, Maryland. Dr. Hanley is coordinating this trial on behalf of the doctors and staff at approximately 40 other hospitals and academic centers in the U.S. and Europe, including your doctor and hospital. He is assisted by a number of organizations and individuals who provide services in support of this trial. The term “sponsor” includes:

- Dr. Hanley;
- his staff at Johns Hopkins; and
- the other people and organizations who assist Dr. Hanley with this study.

It will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study drug may be considered for approval.

Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- The sponsor;
- The U.S. Food and Drug Administration (FDA);
- Department of Health and Human Services (DHHS) agencies;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Genentech, Inc. (the pharmaceutical company providing the drug for this study);
- Johns Hopkins University; and
- [Add local IRB and any additional names here].

The people working on this study will collect information about you. This includes things learned from the procedures described in this consent form. They may collect other information including your name, address, date of birth, and other details. The research team will need to see your information. Sometimes other people at [YOUR INSTITUTION] may see or give out your information. These include people who review the research studies, their staff, lawyers, or other [YOUR INSTITUTION] staff.

The doctors and scientists participating in this study intend to use the information to write medical papers and make presentations at annual meetings. Your identity will not be disclosed in these presentations and publications.

People outside of [YOUR INSTITUTION] may need to see your information for this study. Examples include government groups (such as the Food and Drug Administration), safety monitors, other hospitals in the study, and companies that support the study.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. Information, which may include copies of your medical records, will be delivered by mail, courier, fax transmission, e-mail attachment or by submission to a secure website.

Release of your records is necessary for you to participate in this investigational study. If you do not wish to participate, you will still receive full routine medical care.

**MISTIE:**

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- The sponsor;
- The U.S. Food and Drug Administration (FDA);
- Department of Health and Human Services (DHHS) agencies;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Genentech, Inc. (the pharmaceutical company providing the drug for this study);
- Johnson & Johnson (the medical device company providing the drain tubes for this study);
- Wayne State University (fluid sample testing);
- Johns Hopkins University; and
- [Add local IRB and any additional names here].

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- The U.S. Food and Drug Administration (FDA);
The people working on this study will collect information about you. This includes things learned from the procedures described in this consent form. They may collect other information including your name, address, date of birth, and other details. The research team will need to see your information. Sometimes other people at [YOUR INSTITUTION] may see or give out your information. These include people who review the research studies, their staff, lawyers, or other [YOUR INSTITUTION] staff.

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