INTERCENTER AGREEMENT
BETWEEN
THE CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
AND
THE CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

In 1982, an agreement detailed the working relationships between the organizations previously identified as the Bureau of Medical Devices (BMD), the Bureau of Radiological Health (BRH) and the Bureau of Biologics (BoB) to identify the responsibilities of each for medical device activities.

Since then there have been several major organizational changes within the Food and Drug Administration (FDA). In 1982, BMD and BRH were joined administratively to form the Center for Devices and Radiological Health (CDRH). Also in 1982, BoB and the Bureau of Drugs were merged to form the Center for Drugs and Biologics (CDB), with biological products regulated by the Office of Biologics Research and Review (OBRR). In 1987, however, CDB was split into two major Centers, with biological products regulated by the Center for Biologics Evaluation and Research (CBER).

There also have been major advances in medical device technology and significant changes in the applications for existing technologies. New categories of *in vitro* diagnostic products have been developed to detect evidence of transfusion-transmitted agents that were not recognized in 1982; use of "cellular" biologicals has continued to evolve as a therapeutic practice; and monoclonal antibodies are used in conjunction with medical devices for therapeutic purposes. Thus, this agreement has been updated to include medical devices which were not specified in the previous agreement and developing medical devices and device technologies for which there are no previous jurisdictional guidelines.

This document, which supersedes all prior agreements, outlines the working relationships that exist between CBER and CDRH for certain categories of medical devices or specified medical devices.

Submissions and inquiries should be made directly to the lead Center identified throughout this document.

Inquiries regarding this Agreement should be addressed to:

Jerome A. Donlon, M.D., Ph.D.
Center for Biologics Evaluation and Research (HFB-200)
Food and Drug Administration
8800 Rockville Pike
Bethesda, MD 20892
(301-295-8407)

Leighton W. Hansel
Center for Devices and Radiological Health (HFZ-340)
Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850
(301-427-1311)

I. EFFECTIVE DATE

This document takes effect October 31, 1991.

II. GENERAL DESCRIPTION

The Center for Devices and Radiological Health is designated the lead Center in FDA for regulating medical devices and radiation-related medical devices to ensure their safety and effectiveness. The Center for Devices and Radiological Health will use the device authorities of the Food, Drug and Cosmetic Act (FD&C Act) and the Electronic Product Radiation Control requirements of the Act, as well as any other authorities delegated to it, as appropriate, for devices regulated in that Center.

The Center for Biologics Evaluation and Research is designated the lead Center in FDA for regulating certain medical devices utilized in or indicated for the collection, processing or administration of biological products to ensure their safety and effectiveness and will use authorities under the Public Health Service Act (PHS Act) and the FD&C Act, as well as any other authorities delegated to it, as appropriate. Specific criteria for identifying medical devices regulated by CBER may be found in Section VI. For products that are combinations of biologicals and devices, the designation of the Center with primary jurisdiction is based on the product's primary mode of action.

The Centers will coordinate their activities in order to apply the Medical Devices Authorities in a consistent manner.

III. PROGRAMS THAT CDRH WILL ADMINISTER

The Center for Devices and Radiological Health is designated the Center for major policy development and for the promulgation and interpretation of procedural regulations for medical devices under the FD&C Act. The Center for Devices and Radiological

Health regulates all medical devices, inclusive of radiation-related devices, that are not assigned categorically or specifically to CBER. In addition, CDRH will independently administer the following activities (references to "Sections" are the provisions of the FD&C Act):

1. Small business assistance programs under Section 10 of the Amendments (See PL 94-295). Both CBER and CDRH will identify any unique problems relating to medical device regulation for small business;

2. Registration and listing under Section 510. CBER will receive printouts and other assistance, as requested;

3. Color additives under Section 706, with review by CBER, as appropriate;

4. Good Manufacturing Practices (GMP) Advisory Committee. Under Section 520(f)(3), CBER will regularly receive notices of all meetings, with participation by CBER, as appropriate;

5. Medical Device Reporting. The manufacturers, distributors, importers, and users of all devices including those regulated by CBER, shall report to CDRH under Section 519 of the FD&C Act as required. CDRH will provide monthly reports and special reports as needed to CBER for investigation and follow-up of those medical devices regulated by CBER.

IV. PROGRAMS THAT CBER AND CDRH WILL ADMINISTER

Both CBER and CDRH will administer and, as appropriate, enforce the following activities for medical devices, including their components, parts, and accessories, assigned to the respective Centers (references to "Sections" are the provisions of the FD&C Act):

1. Surveillance and compliance actions involving general controls violations, such as misbranded or adulterated devices under Sections 301, 501, and 502;

2. Warning letters, seizures, injunctions, and prosecutions under Sections 302, 303, and 304;

3. Civil penalties under Section 303(f) and administrative restraint under Section 304(g);

4. Non-regulatory activities, such as educational programs directed at users, participation in voluntary standards organizations, etc.;

5. Promulgation of performance standards and application of special controls under Section 514;

6. Premarket Notification, Investigational Device Exemptions including Humanitarian Exemptions, Premarket Approval, Product Development Protocols, Classification, Device Tracking, Petitions for Reclassification, Postmarket Surveillance under Sections 510(k), 513, 515, 519, 520 (g) & (m), and 522, and the advisory committees necessary to support these activities;

7. Banned devices under Section 516;

8. FDA-requested and firm-initiated recalls whether under Section 518 or another authority and other Section 518 remedies such as recall orders;

9. Exemptions, variances, and application of CGMP regulations under Section 520(f):

10. Government-Wide Quality Assurance Program; and

11. Requests for export approval under Sections 801(e) and 802.

V. SUBMISSIONS

According to the guidance presented in Section VI of this document, statutory submissions such as 510(k)s, IDEs, PMAs, are to be made directly to the appropriate Center. For those medical device systems that are identified in Section VI as involving more than one Center, the submission should be made to the lead Center. Submissions should be made to the appropriate Center at the addresses provided below:

For Devices Regulated by CBER:

Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Product Certification (HFB 240)
8800 Rockville Pike
Bethesda, MD 20892

For Devices Regulated by CDRH:

Food and Drug Administration
Center for Devices and Radiological Health (HFZ 401)
1390 Piccard Drive
Rockville, MD 20850

For submissions involving medical devices and/or biological products that are not addressed in this Agreement, sponsors are referred to the product jurisdiction regulations (21 CFR Part 3). These procedural regulations have been promulgated to facilitate the determination of regulatory jurisdiction but do not exclude the possibility for a collaborative review between the Centers.

VI. MEDICAL DEVICES FOR WHICH THE CENTER FOR BIOLOGICS EVALUATION AND RESEARCH WILL HAVE LEAD RESPONSIBILITY

In general, CBER will have the lead responsibility for regulating medical devices used or indicated for the collection, processing, storage or administration of blood products, blood components or analogous products, as well as screening or confirmatory clinical laboratory tests associated with blood banking practices and other process testing procedures. In vitro tests which are required for blood donor screening and related blood banking practices (such as donor re-entry) are licensed under the PHS Act (refer to the list in Section B1).

The Center for Biologics Evaluation and Research also has the responsibility for regulating all in vitro tests (including diagnostic tests which are not performed in association with blood bank practices) and any other medical devices intended for use for human immunodeficiency virus, type 1 (HIV 1) and type 2 (HIV 2) and other retroviruses. These devices, including (but not limited to) collection devices, specimen containers, test kit components or support materials and those used or indicated for the inactivation of these viruses, will be regulated by CBER under the Medical Device Authorities. For a product that is a combination of a device and a biological, the determination of the Center of primary jurisdiction is based on the primary mode of action.

A. Medical devices regulated by CBER through the use of the Medical Device Authorities:

1. Medical devices which are dedicated systems intended for use with human subjects in the collection, processing, and/or administration of an in vivo use licensed biological or analogous product which are marketed separately from the licensed biological or analogous product. For example, this would include plasmapheresis machines used to collect, process and/or administer a licensed biological product and filters used to prepare a biological product. This category does not include blood administration sets, including those administration sets with filters, which are regulated by CDRH.

   This category also excludes medical devices intended for direct therapeutic application, which will be regulated by CDRH. Direct therapeutic application is defined as the use of a particular medical device for a particular patient with a specific disease or medical condition where the application of such a device is

intended to produce a direct clinical benefit to the patient. This would, for example, include medical devices applied to remove toxic substances or excess cells for a therapeutic benefit, blood administration sets and intraoperative blood salvage devices.

2. Certain *in vitro* reagents including:

   a. those intended for use in the processing of licensed biologicals and analogous products including but not limited to lectins, protectins, bovine albumin and potentiating media,

   b. quality assurance reagents intended for use in conjunction with licensed biological reagents or *in vitro* tests,

   c. leukocyte typing sera or other medical devices intended for use in the determination of tissue type.

3. Medical devices other than reagents intended for use in the preparation of, in conjunction with, or for the quality assurance of a blood bank related licensed biological product or practice. Examples include: clinical laboratory devices with separate blood bank claims, software for clinical laboratory devices with separate blood bank claims, software programs for data management in a blood establishment, dosimeters and thermal indicators that are used for licensed biological products and microwave ovens used for thawing blood products. CDRH will continue to be responsible for administering the Electronic Product Radiation Control provisions of the Act.

B. Medical devices regulated by CBER under the PHS Act[1]:

1. *In vitro* reagents subject to licensure including:

- Antibody to Hepatitis B Surface Antigen
- Antibody to Human Immunodeficiency Virus Type 1
- Anti-Human Globulins
- Blood Grouping Reagents
- Hepatitis B Core Antigen
- Hepatitis B Surface Antigen
- Hepatitis C Virus Encoded Antigen
- Human Immunodeficiency Virus Type 1
- Human Immunodeficiency Virus Type 2
- Human T-Lymphotropic Virus Type I
- Limulus amebocyte lysate (LAL) for either manufacturing or clinical diagnostic use
- Reagent Red Blood Cells

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[1] Certain drug provisions of the FD&C Act may be applied.

CBER may also regulate, as a licensed biological, any *in vitro* biological test reagent or reagent test which may be required to ensure the safety of blood, blood products or analogous products, or to ensure the purity, potency and safety of other licensed products.

2. Certain combinations of medical devices and biological products including:

   a. medical devices intended to serve as delivery systems for licensed biologicals which are packaged with a licensed biological (e.g., allergen patch and "tine" tests),

   b. medical devices which are filled with licensed biologicals as a part of the manufacturing process, (prior to marketing to the end user) that are intended to serve as the final container and delivery system for the licensed biological (e.g., syringes filled with Rh,D immunoglobulin),

   c. medical devices intended to serve as *in vivo* delivery systems or implants for licensed biologicals which are either impregnated with a licensed biological or combined with a licensed biological as part of the manufacturing process

C. Special Situations

1. *In vitro* tests or reagents for the direct or indirect detection of infectious agents such as cytomegalovirus, *Yersinia enterocolitica*, those causing syphilis and chagas disease and any other infectious agents that are transmitted by blood, blood products or analogous products will be assigned to CBER and CDRH as follows:

   a. when such tests or reagents are intended only for diagnostic use, CDRH will regulate under the Medical Device Authorities (MDA),

   b. when such tests or reagents are intended for only for blood and plasma donor screening, CBER will regulate under MDA,

   c. when such tests or reagents are intended for both diagnostic use *and* blood and plasma donor screening, CDRH will have the lead. Each Center will review the data necessary to support the intended use claims for which they have regulatory authority. Consolidated responses will be made to submissions or inquiries.

   d. when such tests or reagents are required by the Agency for use in blood banks and plasmapheresis centers, CBER will regulate under the PHS Act.

2. Nonlicensed human source materials of blood and blood components, intended for use in the manufacture of unlicensed in vitro diagnostic devices (including reagents) will be regulated by CBER during collection, storage and initial processing. Once the component materials have been incorporated into a manufacturing step whereby they are irrecoverable as original material or are packaged in a device container, these component materials become the regulatory responsibility of CDRH and will be regulated as medical devices under the Medical Device Authorities.

3. Automated cell separators and other blood processing equipment will be regulated as medical devices under the Medical Device Authorities.

    a. CDRH will have the lead responsibility if the medical device is used for therapeutic purposes. Therapeutic purposes is defined as the application of a particular medical device to a particular patient with a specific disease where the application of such a device is intended to produce a direct clinical benefit through the removal of toxins or excess deleterious elements.

    b. CBER will have the lead responsibility for those medical devices used to separate components for the production of blood products and biological products. This would include devices used to collect, process/manipulate, store or modify particular biological components or "cellular" biologicals such that the benefit to the patient or recipient is derived from the administration of the biological component or "cellular" biological.

    c. If automated cell separators or other blood processing equipment may be used for either therapeutic purposes or for the purpose of separating components for the production of blood products, CDRH will have the administrative lead responsibility. Each Center will review respective clinical and scientific data according to claimed uses. Consolidated responses will be made to submissions or inquiries.

4. Medical devices that are intended for use in the processing of blood and blood components where the medical devices either include or are used in conjunction with filters, columns and other matrices (such as magnetic beads) that are coupled with biological substances (such as monoclonal antibodies) will be regulated as follows:

    a. CDRH will have the lead responsibility if the devices are used for therapeutic purposes (as

discussed in A.1.) and CBER will be consulted for decisions involving the biological substance.

b. CBER will have the lead responsibility if the devices are used for the collection, separation or processing of components for the production of blood, blood products, biological products, analogous products or "cellular" biologicals.

Bone marrow is considered a biologic analogous to blood or blood components. Any device or reagent used in the collection, processing or storage of bone marrow will be regulated by CBER. CBER has the option of regulating bone marrow directly through the licensing process and/or regulating the devices and reagents associated with bone marrow processing by use of the Medical Device Authorities.

5. Irradiators intended for use in the inactivation of immunologically active cells in whole blood, red blood cells and platelets will be regulated by CDRH with consultation by CBER on the safety and effectiveness of the irradiated product.

Irradiators intended for use in the in-process inactivation of HIV viruses or other pathogens in all blood products, licensed biological products, or analogous products will be regulated by CBER with consultation by CDRH.

6. CDRH will regulate tissue processing equipment and solutions used for transporting, storing, or otherwise processing human tissues and organs except for the equipment and solutions related to biological products.

Cultured skin will be regulated by CDRH under the Medical Device Authorities. Cellular and tissue implants, including infused cells and encapsulated cells or tissues, will be regulated by CBER under the PHS Act and the FD&C Act (as amended), as appropriate.

VII. GENERIC DEVICES FOR WHICH CBER WILL HAVE LEAD RESPONSIBILITY

CBER is the lead Center for the classified generic devices listed in the chart below. Under the chart headings, the "Product Code" is a five character code assigned to a device or generic group of devices for use by manufacturers to list devices with FDA. The first two characters identify the classification advisory panel which provided a classification recommendation to FDA. If a PMA number is noted, there is no classification regulation. A breakdown of panel codes is as follows:

81 Hematology
83 Immunology

"Name" is the name used by CDRH in its product code book to describe a generic category of device.

"Section" is the section in Title 21 of the Code of Federal Regulations under which the regulation classifying the device is codified.

"Regulation Name" is the name that was used in publishing the classification regulations.

Product Code	Device Name	Section	Regulation Name
81 GKT	Automated Blood Cell Separators	864.9245	Automated Blood Cell Separator
81 KSB	Transfer Sets	864.9875	Transfer Sets
81 KSD	Heat Sealing Devices	864.9750	Heat Sealing Devices
81 KSE	Blood Storage Refrigerators and Freezers	864.9700	Blood Storage Refrigerators and Freezers
81 KSF	Quality Control Kits for Blood Banking Reagents	864.9650	Quality Control Kit for Blood Banking Reagents
81 KSG	Potentiating Media for in vitro Diagnostic Use	864.9600	Potentiating Media for in vitro Diagnostic Use
81 KSH	Environmental Chambers for Storage of Platelet Concentrate	864.9575	Environmental Chamber for Storage of Platelet Concentrate
81 KSI	Lectins and Protectins	864.9550	Lectins and Protectins
81 KSK	Stabilized Enzyme Solutions	864.9400	Stabilized Enzyme Solution
81 KSL	Copper Sulfate for Specific Gravity Determination	864.9320	Copper Sulfate Solution for Specific Gravity Determinations
81 KSM	Automated Coombs-Test Systems	864.9300	Automated Coombs Test System
81 KSN	Automated Cell-Washing Centrifuges for Immunohematology	864.9285	Automated Cell-Washing Centrifuge for Immunohematology
81 KSO	Blood Bank Centrifuges for in vitro Diagnostic Use	864.9275	Blood Bank Centrifuge for in vitro Diagnostic Use
81 KSP	Cell-Freezing Apparatus and Reagents	864.9225	Cell-Freezing Apparatus and Reagents for in vitro Diagnostic use
81 KSQ	Blood Mixing and Weighing Devices	864.9195	Blood Mixing Devices and Blood Weighing Device
81 KSR	Empty Containers for the Collection & Processing of Blood and Blood Components	864.9100	Empty Container for the Collection and Processing of Blood and Blood Components
81 KSS	Blood Bank Supplies	864.9050	Blood Bank Supplies
81 KST	Vacuum-Assisted Blood Collection Systems	864.9125	Vacuum-Assisted Blood Collection System
81 KSW	Processing Systems for Frozen Blood	864.9145	Processing System for Frozen Blood
81 KSX	Blood Grouping Substances of Non-human Origin for in vitro Diagnostic Use	864.9160	Blood Grouping Substances of Nonhuman Origin for in vitro Diagnostic Use
81 KSY	Blood Grouping View Boxes	864.9185	Blood Grouping View Box
81 KSZ	Automated Blood Grouping and Antibody Test Systems	864.9175	Automated Blood Grouping and Antibody Test System
81 KZL	Blood and Plasma Warming Devices	864.9205	Blood and Plasma Warming Device
	Test, Hepatitis B Core (IgM)	PMA	

VIII. INTERCENTER JURISDICTIONAL COMMITTEE

An intercenter jurisdictional committee is now formed. It is composed of one representative and one alternate from each Center. The committee members will meet on an ad hoc basis, will discuss all jurisdictional questions and will be expected to handle the majority of requests for jurisdiction assignments. Where this committee cannot agree upon jurisdictional assignment, or where the sponsor requests review of assignment at the agency level, the product jurisdiction procedures will be used.

Gerald V. Quinnan, Jr., M.D.
Acting Director
Center for Biologics Evaluation and Research

10/31/91
Date

James S. Benson
Director
Center for Devices and Radiological Health

10/31/91
Date

Concur:

David A. Kessler, M.D.
Commissioner of Food and Drugs