Center for Veterinary Medicine: Electronic Submissions System

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Center for Veterinary Medicine

presented at:

DIA Document Management Conference
FDA Panel Discussion

February 14, 2002

Overview of Electronic Submissions in CVM

- Started with Pilot for proof of concept
- Started with simple reporting requirement as e-mail submissions
- Standardized format
- Workflow and review same as paper
- Worked with industry to set standards

eSubs: Email Program Standards

- Agency Certification
- Center Registration – both paper and electronic
  - Bridge to paper records and test electronic communications
  - Username: email address
  - Password
    - Initially declared by company
    - Initialized in the Center's ES system
    - Changed by the user before submitting
- Email ES System is subject line driven
  - Specified business processes

eSubs: Email Program Standards

- ElEmailnic submission
  - Guidance and Form
  - Single PDF file
  - Encrypted with user password
  - Sent to CVMDCU@cvm.fda.gov
- CVM Processing
  - Checks sender(username), subject line, number and type of files
  - Decrypts, stores and sends information to review system

eSubs: Program Inception

- Started email submissions with drug shipments
  - CVM has received over 3000 electronic NCIEs since 1997
- Prototype program
  - PDF Attachment to formatted email message
  - Manual processing for STARS tracking database logging
  - Manual notification of reviewer by email
  - Modeled the paper process

CVM Review Times (days)

Paper vs. Electronic

First 3 months

	Paper	Electronic
Count	170	213
Average	31.8	10.6
Median	36.0	8.0
Minimum	3	0
Maximum	121	54

Pilot Evaluation

- When compared to paper NCIEs for the same sponsors and INADs for the preceding 3 months:
  - Reduced CVM review time (further improvement over time)
  - Improved overall response time during pilot
  - Receipt for submissions to the sponsors

Observations During Pilot

- Industry liked the electronic format and form, and ease of transport (after adapting changes in internal processes)
- CVM reviewers like the consistent format of e-NCIEs and electronic processing forms
- Training was responsible for success within CVM and industry

Center/Industry Success Story

- Worked with Industry
- Reduced Paper Load (CVM and Industry)
- The First Step toward a Paperless Center
- Reduced Median Processing Time

eSubs: Recent Expansion

- Expanded to other types of info in February 2001
  - Meeting Requests, Final Disposition, Slaughter Notices
  - Guidance and Flat PDF file published on web page
- Smart forms available in June 2001
  - All four types of email submissions
  - Adds Quality Control at submitting industry
  - Automatically logs submissions and forwards for review (Oracle Tracking Database)
  - Automated notification of receipt and errors
  - Upgraded reviewer interface

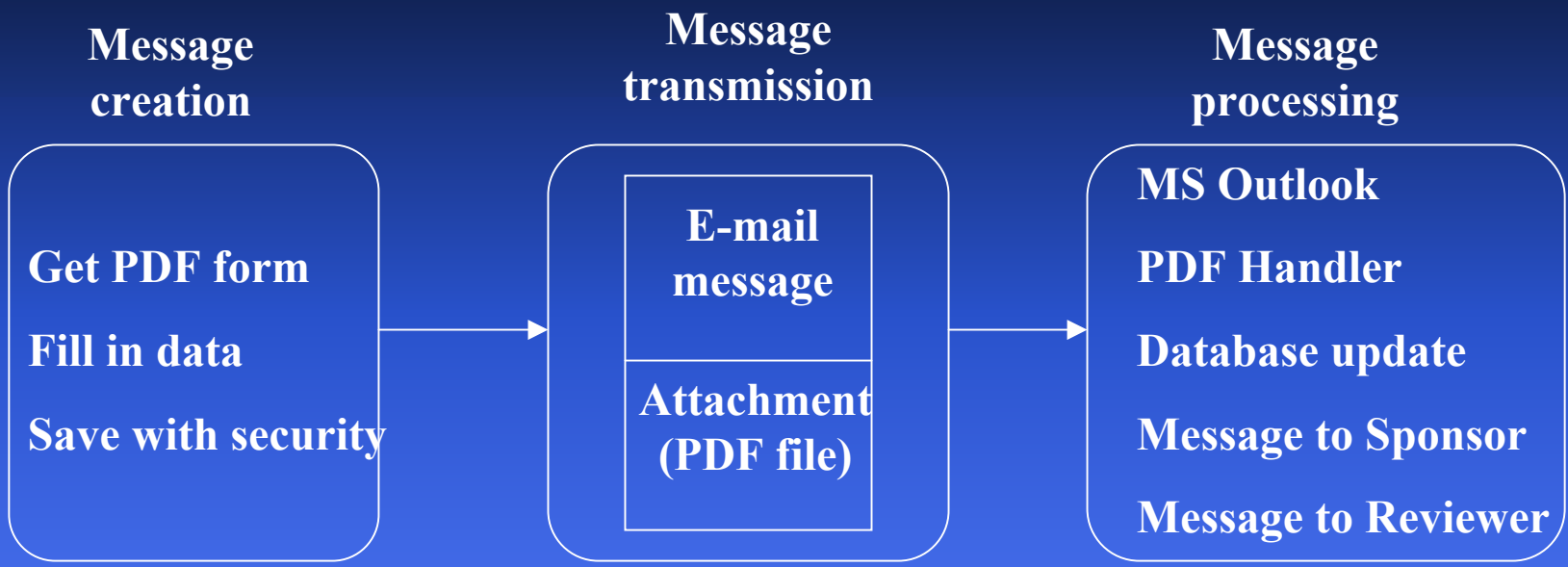
E-Submissions
Email Subject Lines

Subject Line	**Type of Electronic Submission**
NCIE	Notice of Claimed Investigation Exemption
SLAUGHTER	Notice of Intent to Slaughter for Human Food Purposes
DISPOSITION	Notice of Final Disposition of Animals Not Intended for Immediate Slaughter
MEETING	Request for a Meeting or Teleconference to the Office of New Animal Drug Evaluation

Process Changes
E-Mail Subject Lines

Subject Line	**Type of Electronic Submission**
REGISTER	Registration Letter for identification of sponsors and authorized contacts
CHANGE	Changes in conditions of registration, e.g., new contacts, gateway name change, etc.
PASSWORD	Change of individual password after initialization of CVM's Electronic Submission System
ECHO	Test for users to see if CVM's system is up

Current CVM E-Subs Process



Message Creation

- Download Form from CVM Website
  - Or recover from storage area
- Enter appropriate data
- Save with security
  - Supply unique filename
  - Encrypt with password registered at CVM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Veterinary Medicine

NOTICE OF CLAIMED INVESTIGATIONAL EXEMPTION

Form Approved: OMB No. 0910-0117
Expiration Date: 1/31/02

PAPERWORK REDUCTION ACT STATEMENT: A Federal agency may not conduct or sponsor, and a person is not required to respond to, a collection of information, unless it displays a current valid OMB control Number. The public reporting burden for the collection of information is estimated to vary from 15 minutes to 2 hours, with an average of 30 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary information, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information to the Food and Drug Administration, Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

Submit this notice electronically to:
Food and Drug Administration
Center for Veterinary Medicine (HFV- 1)
7500 Standish Place
Rockville, Maryland 20855
(E-mail:cvmdcu@cvm.fda.gov)

DATE: 01/01/2001
INAD / IFA NO: INAD 0
STUDY / TRIAL ID: Study ID
DRUG SHIPMENT NO: Number of this shipment
TYPE OF SHIPMENT: ☐ Initial ☐ Supplement ☐ Discontinued ☐ Other

The sponsor, COMPANY NAME, submits a notice of claimed investigational exemption for the shipment or delivery of a new animal drug under the provisions of 21 CFR 511.1. This information is submitted in electronic form.

I. Shipment ☐ or Receipt ☐ Information

Add Password | Mail to | Reset

1. NAME(S) OF THE DRUG(S)
   Established name(s): Established Name of Drugs (if multiple, please separate by commas)
   Trade name(s): Trade Name
2. PROPOSED USE OF THE DRUG(S): Indication(s)
3. DATE OF DRUG SHIPMENT (OR RECEIPT): 01/01/2001
4. TOTAL QUANTITY (WT. OR VOL.) AND CONCENTRATION OF DRUG(S) SHIPPED (OR RECEIVED): Quantity of Drug
5. TYPE OF STUDY / TRIAL: Type of Study
6. INTENDED USE OF STUDY OR TRIAL: ☐ Pivotal (intended for support of NADA or ANADA) ☐ Non-pivotal
7. NAME AND ADDRESS OF INVESTIGATOR:
   Investigator Name
   Investigator Address First Line
   Investigator Address Second Line
   Phone Number: (000) 000-0000 City State 00000-0000
8. LOCATION OF STUDY / TRIAL:
   Study Location Address First Line
   Study Location Address Second Line
   City State 00000-0000
9. NAME AND ADDRESS OF STUDY MONITOR:
   Monitor Name
   Monitor Address First Line
   Monitor Address Second Line
   Phone Number: (000) 000-0000 City State 00000-0000
10. APPROXIMATE DATE OF STUDY / TRIAL Start: 01/01/2000 Finish: 01/01/2001
11. PROTOCOL SUBMITTED TO CVM: ☐ Yes ☐ No
    If Yes, date submitted to CVM and/or CVM submission number: 01/01/2001 0
12. SPECIES OF ANIMALS: Animal Production Class
13. SIZE AND TYPE OF ANIMALS: Size and Type of Animals
14. APPROXIMATE NUMBER OF ANIMALS (IN THIS TRIAL):
    Total: 0 Treated: 0 Control: 0
15. NUMBER OF ANIMALS PREVIOUSLY USED:
    Total: 0 Treated: 0 Control: 0
16. MAXIMUM DAILY DOSE: Maximum Dose AND DURATION: Duration of Dosing
17. METHOD OF ADMINISTRATION: Route of Administration
18. CONTRACT RESEARCH ORGANIZATIONS (CRO) USED: ☐ Yes ☐ No
    Name and address of CRO:
    CRO Name
    CRO Address First Line
    CRO Address Second Line
    Phone Number: (000) 000-0000 City State 00000-0000
    Description of obligations transferred to CRO: Description of obligations

Created by: Center for Veterinary Medicine
HFV-016 (301) 827-8277 HP

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Veterinary Medicine

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Submit this notice electronically to:
Food and Drug Administration
Center for Veterinary Medicine (HFV- 102)
7500 Standish Place
Rockville, Maryland 20855
(E-mail:cvmdcu@cvm.fda.gov)

DATE: **01/01/2001**
INAD / IFA NO: **I INAD 0**
STUDY / TRIAL ID: **Study ID**
DRUG SHIPMENT NO: **Number of this shipment**
TYPE OF SHIPMENT: ☐ Initial ☐ Supplement ☐ Discontinued ☐ Other

The sponsor, **COMPANY NAME**, submits a notice of claimed investigational exemption for the shipment or delivery of a new animal drug under the provisions of 21 CFR 511.1. This information is submitted in electronic form.

I. Shipment ☐ or Receipt ☐ Information

Add Password | Mail to | Reset

1. NAME(S) OF THE DRUG(S)
   Established name(s): **Established Name of Drugs (if multiple, please separate by commas)**
   Trade name(s): **Trade Name**
2. PROPOSED USE OF THE DRUG(S): **Indication(s)**
3. DATE OF DRUG SHIPMENT (OR RECEIPT): **01/01/2001**
4. TOTAL QUANTITY (WT. OR VOL.) AND CONCENTRATION OF DRUG(S) SHIPPED (OR RECEIVED): **Quantity of Drug**
5. TYPE OF STUDY / TRIAL: **Type of Study**
6. INTENDED USE OF STUDY OR TRIAL: ☐ Pivotal (intended for support of NADA or ANADA) ☐ Non-pivotal
7. NAME AND ADDRESS OF INVESTIGATOR: **Investigator Name**
   Investigator Address First Line

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Veterinary Medicine

REQUEST FOR A MEETING OR TELECONFERENCE

Form Approved: OMB No. 0910-0452
Expiration Date: 11/30/2003

PAPERWORK REDUCTION ACT STATEMENT: A Federal agency may not conduct or sponsor, and a person is not required to respond to, a collection of information, unless it displays a current valid OMB control Number. The public reporting burden for the collection of information is estimated to vary from 15 minutes to 2 hour, with an average of 60 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary information, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information to the Food and Drug Administration, Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

Submit this notice electronically to:
Food and Drug Administration
Center for Veterinary Medicine (HFV- 100)
7500 Standish Place
Rockville, Maryland 20855
(E-mail:cvmdcu@cvm.fda.gov)

DATE: 02/02/2002
INAD / NADA NO: I INAD 123
DRUG: Sodium Chloride
SPECIES: Dog All

The sponsor, Water Retention Inc. , submits a request for a meeting or teleconference.
This information is submitted in electronic form.

Add Password Mail to Reset

I. Request:

1. PROPOSED DATE(S) AND TIME(S): 04/04/2002 10:00 am
2. SPONSOR PARTICIPANTS:

Dr. Howard, Jones and Alder from our firm

3. REQUESTED CVM PARTICIPANTS:

Ms. Sayer, Health and their branch chief

Message Transmission

- Encrypt PDF file
  - Automated in smart form
- Address email to cvmdcu@cvm.fda.gov
  - Automated in smart form
- Type submission type in the subject line
  - Automated in smart form
- Attach the PDF file of the form to the message
  - Automated in smart form (also encryption)
- Send the message

Message Processing

- MS Exchange program
- PDF Handler program
- Database update program
- Message to Sponsor
- Message to CVM Reviewer

MS Exchange Program

- Detects message in CVMDCU mailbox
- Checks message parameters for correctness
- Notifies CVMSTARS by e-mail
- Stores message in public folder
- Sends extract command to PDF Handler

PDF Handler Program

- Extracts submission attachment
- Runs ARTS security to remove password
- Saves PDF in Archive w/o password
- Exports information to FDF file
- Notifies CVMSTARS of PDF complete
- Calls stored procedure for database update

Database Update Program

- Open the FDF file
- Extracts the fields
- Attaches to STARS database
- Verifies document type & number
- Inserts new submission information

STARS2000 - [Pending Submission Location/Status T2 (PEND_STATUS)]

STARS2001 Exit Quality Control Admin Edit Window Help

Page 1 **PENDING SUBMISSION LOCATION/STATUS** 02/05/2002 T-2

SUBMISSIONS

Document/Submission ID: I 000123 Z 0001 OT Meet/Req Other

Purpose of Submission: REQUEST FOR MEETING FOR 4/4/2002

Referenced Submission:

Referenced DER:

Date Received: 02/04/2002 Clock Reset Date:

Primary Branch: HFV-100

Primary Reviewer: UNASSIGNED

Meeting Date: 04/04/2002

Review Days, Total: 1 DCU: 0 SCI: 1 ADM: 0

Corr Date: 02/02/2002

Volumes: 0 - 0

CVM Due Date: 05/24/2002

Date Into Branch: 02/04/2002

Review Status: SCIENTIFIC

Admin. Org.:

ELECTRONIC SUBMISSIONS

CVM Archive Filename : Q:\2002\02Feb\02-04\CVM200202040010.PDF

PENDING REVIEWS

Branch	Reviewer	Amendment		Package	Date In	Date Due	Days Pending	Days Overdue

Report Overview Comp Revs/Amend Movements Exit

Press Ctrl+E or doubleclick to display entire field.

Record: 1/1

Start O.. G.. A.. u.. Mic... 2.. T.. S. 1:41 PM

Receipt Message to Sponsor

- Fetches Receipt Form (PDF Form)
- Populates Form
- Saves Form in the Archive
- Encrypts Form with password
- Sends Form as e-mail attachment

Sponsor Receipt

The Center for Veterinary Medicine, Food and Drug Administration acknowledges the receipt of your submission to the FDA CVM Electronic Submission System. The following information has been entered into our tracking system and your submission has been forwarded to our review division.

I-000123-Z-0001

Correspondence Date: 02/02/2002
CVM Received Date: 02/04/2002
CVM Due Date: 05/24/2002
Consulting Due Date: 05/12/2002

Applicant: Water Retention Inc.

Document Type: INVESTIGATIONAL NEW ANIMAL DRUG
Applicant Drug: Sodium Chloride

Expedited Status: N

Submission Type: REQUEST FOR MEETING
Sub Classification: OTHER; UNCLASSIFIED

Purpose of Submission:

Parent Submission (if amendment):
In Reference to Submission:
CVM Message Identifier: CVM200202040010
Sponsor File: meeting_ex1.pdf
Review Division: HFV-100
Reset Clock Date (if applicable):
Meeting Date (if meeting): 04/04/2002

If you have any questions, please contact either the review division or the Electronic Submission Coordinator at 301-827-8277.

Review Message to Reviewer

- Extracts information from submission
- Populates MS Outlook form
- Sends Outlook Form by e-mail to Review Division mailbox for assignment
  - Routing form
  - Link to submission stored on LAN
  - Models review and oversight business rules
  - Final action form (attach review and letter)

ES Reviewer Notification for I-000123-Z-0001 - CVM ES Reviewer (Plain Text)

File Edit View Insert Format Tools Actions Form Layout Help

Message | Information

From: CVM PDF Extraction Process

Sent: Mon 2/4/2002 1:40 PM

To:

Subject: ES Reviewer Notification for I-000123-Z-0001

Submission Forwarded

CVM Electronic Submissions Reviewer Notification Form

ES Notification Information

Submission ID: I-000123-Z-0001

Purpose:

Document Type: INVESTIGATIONAL NEW ANIMAL DRUG

Submission Type: REQUEST FOR MEETING

Drug: CHLORPHENIRAMINE MALEATE

Applicant Information

Applicant: CENTER FOR VETERINARY MEDICI

Submitted: HRrascal@aol.com

Email: HRRascal@aol.com

Correspondence Date: 02/02/2002

Received Date: 02/04/2002

CVM Information

Team: HFV-100

CVM Due Date: 05/24/2002

Meeting Date: 04/04/2002

Expedited: N

Final Action Information

Type: Meeting

FNR | Reset

FNR/w Memo | ACK

Add Attachment

View Information

Submission

Comments | History | Sys Message

Commands

Forward | Rqst Concur | Return | Concur | Final Action

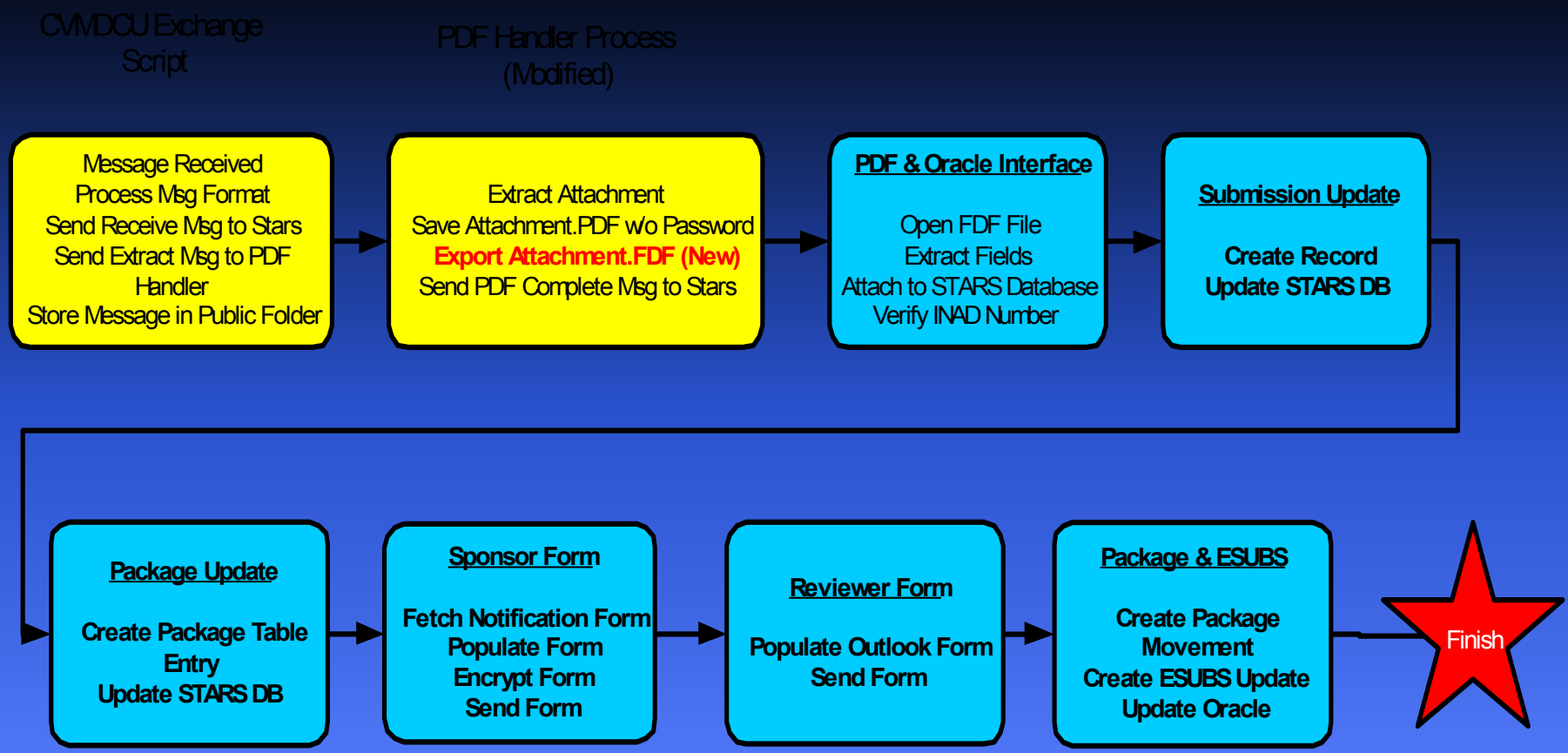
Message Text

5.3.12

Reviewer Notification Form requires action to be taken.

Start | 1:47 PM

Smart PDF Form Processing



Integrity Aspects

- Separation of processes
- Extensive log files for processing steps
- Archive of e-mail
- Backup at daily intervals
  - Exchange
  - PDF handler
  - Oracle database

Security Aspects

- Automated processing
- Protected archive area
- Database audit trails
  - Restricted updates & deletions saved
  - Log of all commands and actions
- Fact of processing
  - Validates message integrity

Security Awareness

- Information Systems Security (INFOSEC)
  - Assessment by NSA in January 1999
- Conclusions
  - Good overall security
  - Finding of no legal agreement
- Registration procedure satisfies legal agreement

Electronic Submissions Volume as of 2/4/2002

Sub Type	Total Rec'd	Smart (7/27/01)	Regular (7/27/01)
NCIE	3205	37	414
Meeting	14	9	3
Disposition	19	9	5
Slaughter	3	0	0

eSubs: Initiative 1

- Expanding eSubs to larger, hard-media submissions
  - Reference on Agency docket to accept hard media submissions
    - Currently using CDER guidance as reference
    - Preparing CVM specific guidance
- Resources allocated to develop prototype
  - Secure archiving on LAN
  - Tracking in STARS
  - Access through reviewer interface
  - Same performance standards as paper-based submissions

eSubs: Initiative 2

- Expanding eSubs to receive bulk data
  - XML for data in Annual DER reports
    - Adverse Drug Experience periodic reporting
    - Automated data loading for current review module
  - Smart Form 1932 for ADE submissions
  - XML submissions for manufacturing stability data
    - Standards developed in conjunction with CDER
    - Adaptation of CDER's prototype
    - Pre-approval evaluation
    - Post marketing reporting

Electronic Review Environment

- CDMS (Corporate Document Management System)
  - Knowledge management
  - Interface for reviewer processes
  - Workflow modeling and automation
  - Electronic records
  - Electronic signatures
  - Connection to data applications

Electronic Submissions Project

The Center for Veterinary Medicine (CVM), has developed and implemented methods to accept electronic files as legal, original submissions for review. This extraordinary step was made possible by the publication of FDA's Final Rule on Electronic Records and Electronic Signatures (21 CFR Part 11) in March 1997, which set the standards for Electronic Records for FDA and its regulated industries.

The Center began with an Electronic Submission Pilot Project to determine the practicality of the electronic submission and review of electronic information as an alternative to the current paper-based processes. CVM started by allowing sponsors to submit Notices of Claimed Investigational Exemption (NCIE), often referred to as drug shipment notices, as PDF attachments to e-mails via the Internet. See ***FDA Announces A Pilot Project For NCIE Submission***. Specific information on how to register to submit information to the Center is contained in
How to Use E-Mail to Submit Information to The Center for Veterinary Medicine Final Guidance |pdf| |doc| . The NCIE submission was selected for the initial pilot because of its simplicity, size, and broad use by CVM and the regulated industries.

Anyone sending in electronic submissions to the Center by e-mail must first register and follow all requirements in the ***How to Use E-Mail to Submit Information to The Center for Veterinary Medicine Final Guidance*** |pdf| |doc| .

Information and forms for the accepted reporting-type submissions are:

Notices of Claimed Investigational Exemption

- Guidance # 59
- Notice of Availability of Guidance in the Federal Register
- Word
- PDF
- PDF Fill-in

Meeting Requests and Agendas

- Guidance# 88
- Notice of Availability of Guidance in the Federal Register
- Word
- PDF
- PDF Fill-in

Notices of Final Disposition of Slaughter for Human Food Purposes

A View into the Future

- Totally integrated CVM process
  - Pre and post-marketing information
  - Data submitted electronically
  - Data available for review
  - Historical data available online
  - Electronic review
  - Automated workflow
  - Storage and retrieval of information
  - Web-based communication