

- The number of lines of program code in the Chemistry module, excluding comments, is on the order of 150 000.
- (2) Chemical Abstracts Service (Columbus, OH) and VSE Corp. (Alexandria, VA) participated in separate contracts with NCI. The contract with CAS ended in 1985; VSE continues to provide support to NCI in the biological data processing area.
 - (3) Heller, S. R.; Milne, G. W. A.; Feldmann, R. J. "A Computer-Based Chemical Information System". *Science (Washington, D.C.)* **1977**, *195*, 253-259. Milne, G. W. A.; Heller, S. R.; Fein, A. E.; Frees, E.; Marquart, R.; McGill, J. A.; Miller, J. A.; Spiers, D. S. "The NIH-EPA Structure and Nomenclature Search System". *J. Chem. Inf. Comput. Sci.* **1978**, *18*, 181-186. In 1984, the NIH-EPA Chemical Information System, which includes SANSS, was transferred into the private sector. It is currently offered by two vendors (CIS, Inc., Baltimore, MD, and Information Consultants Inc., Washington, DC).
 - (4) The first operational version of SANSS was completed in 1976 and made available for public use as a part of the NIH-EPA Chemical Information System. It has been used continuously since then by well over 1000 fee-paying users.
 - (5) The question of time per structure is discussed in part 2 of this series of papers. With the touch-pen method, a typical structure can be entered in under 3 min. The keyboard-entry program reduces this to less than 1 min.
 - (6) Versatec, Inc., a Xerox Co., is located at 2805 Bowers Avenue, Santa Clara, CA 95051.
 - (7) Friedman, N. K. "Japanese Word Processing: Interfacing with the Inscrutable". *Abacus* **1986**, *3*, 34-42.
 - (8) Dittmar, P. G.; Mockus, P.; Cuvreur, K. M. "An Algorithmic Computer Graphics Program for Generating Chemical Structure Diagrams". *J. Chem. Inf. Comput. Sci.* **1977**, *17*, 186-192.
 - (9) Milne, G. W. A.; Feldman, A.; Miller, J. A.; Daly, G. P.; Hammel, M. J. "The NCI Drug Information System. 2. The DIS Pre-Registry". *J. Chem. Inf. Comput. Sci.*, preceding paper in this issue.
 - (10) Systems offering nomenclature searching with no structure searching include Lockheed's DIALOG, NLM's CHEMLINE, and Burrough's SDC/ORBIT and BRS. Both nomenclature and structure searching are supported by SANSS and by CAS ONLINE. The service provided by DARC/QUESTEL is primarily a structure search and does not include nomenclature searching.
 - (11) Richman, S.; Hazard, G. F.; Kailkow, A. K. "The Drug Research and Development Chemical Information System of NCI's Developmental Therapeutics Program". In *Retrieval of Medicinal Chemical Information*; Howe, W. J., Milne, M. M., Pennell, A. F., Eds.; ACS Symposium Series 84; American Chemical Society: Washington, DC, 1978; pp 200-221.
 - (12) The DIS allows retrievals based upon the full molecular weight (MW), which contains all the addend molecular weights. Retrievals are also allowed on the molecular weight of any particular addend (MWAD).
 - (13) A full and precise match at the addend level is required in the IDENT search. Thus aniline will retrieve aniline, aniline hydrochloride, and all other salts of aniline. An IDENT search for aniline butyrate will retrieve only aniline butyrate, but if the search is done with just the butyrate, all butyrates, including aniline butyrate, will be retrieved. The version of IDENT used in the DIS Pre-Registry is more flexible and handles addend discrepancies slightly differently. This is described in more detail in the preceding paper in this series.
 - (14) Ray, L. C.; Kirsch, R. A. "Finding Chemical Records by Digital Computers". *Science (Washington, D.C.)* **1957**, *126*, 814-819.
 - (15) Feldmann, R. J.; Milne, G. W. A.; Heller, S. R.; Fein, A. E.; Miller, J. A.; Koch, B. "An Interactive Substructure Search System". *J. Chem. Inf. Comput. Sci.* **1977**, *17*, 157-163.
 - (16) Seventy-eight different elements are represented at least once in the NCI database. The elements that are not represented are the five noble gases, one lanthanide (promethium), and thirteen actinides (actinium, protactinium, and all elements beyond uranium). This reflects the eclectic approach that has been adopted in the search for anticancer drugs.
 - (17) Feldmann, R. J.; Heller, S. R. "An Application of Interactive Graphics—the Nested Retrieval of Chemical Structures". *J. Chem. Doc.* **1972**, *12*, 48-54.

The NCI Drug Information System. 4. Inventory and Shipping Modules

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The Inventory/Shipping package of the NCI Drug Information System (DIS) is designed to support all inventory and shipping operations associated with the testing by the NCI of large numbers of chemicals for anticancer activity. Two major databases, an Inventory database and a Shipping History database, contain all of the data associated with these operations. Software that supports the operations in an online interactive manner also provides for the accessing and updating of these databases as necessary. Special hardware in the form of barcode reader/printers and digital balances is also interfaced to the system to improve the efficiency of the operations.

INTRODUCTION

In the first part of this series, the general structure of the NCI Developmental Therapeutics Program (DTP), whereby large numbers of chemicals are tested for anticancer activity, was described. As part of this program, a physical inventory of those chemicals is maintained,¹ and shipments of the chemicals are made to screening laboratories² and other recipients³ as necessary in order to perform specified series of tests on the chemicals.

The NCI Drug Information System (DIS), also described in general in the first part of this series, is designed to support the various inventory and shipping operations performed in the course of day-to-day DTP project activities. Support of these operations is primarily interactive, and this support extends to automated laboratory stations, where material is subdivided, weighed, and packaged for shipment. Two major databases are also supported as part of the DIS Inventory/

Shipping module, and these provide Inventory and Shipping History information, respectively, on the chemicals tested under the DTP project.

OVERVIEW

The inventory and shipping operations performed in the course of DTP project activities, all of which are directly supported by the DIS, are illustrated schematically in Figure 1. The major steps in these operations are as follows.

Receipt of Chemicals. All chemicals ordered for screening are received by the NCI acquisitions contractor, who indicates the receipt of the material to the DIS and registers the material with respect to the Chemistry database. New compounds are assigned new NSC Numbers, and additional materials for existing compounds are assigned new sample numbers under those NSC Numbers. This contractor also orders and receives refills of chemicals, as requested by NCI. All received ma-

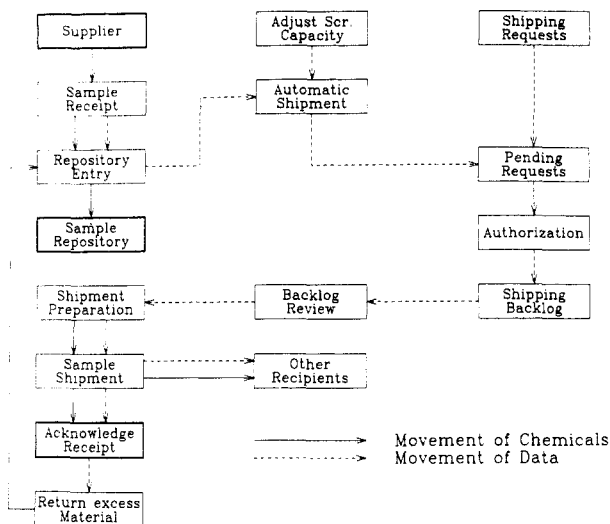


Figure 1. Overview of DIS Inventory/Shipping operations.

terial, from either initial orders or reorders, is then forwarded to another NCI contractor (Storage contractor), who operates the chemical repository. The receipt of material at the repository site is indicated to the system by the Storage contractor. Received material may also be weighed at that time.

Automatic Shipments. All new compounds received at the repository, unless marked to the contrary in some manner,⁴ are eligible to be shipped to a screening laboratory for initial testing. Periodically, the DIS will accumulate these compounds onto automatically generated shipping lists and direct them to the screening laboratories with the largest unused capacity for performing such tests. These "auto-shipments" usually contain 36 different chemicals and currently between 2 and 4 of these are shipped per week. Compounds that are reordered are designated for specific testing and are not shipped automatically with the new compounds. The DIS provides for the automatic shipment of new compounds to screening laboratories for testing, and it is necessary therefore that the flow of chemicals or the available screening capacity can be adjusted so that they match. The DIS allows this by means of a step that permits properly authorized NCI personnel to adjust the capacity of various screening laboratories for accepting such tasks.

NCI-Ordered Shipments. For compounds that show some activity in the initial tests, additional series of tests may be ordered. The shipment of material for these tests is requested through the manual specification of a shipping list containing the items to be shipped. All shipping requests, even those automatically generated by the DIS, constitute government contractual obligations. They must therefore be authorized by one or more NCI officials before the shipment can proceed. A DIS program provides for that authorization.

Shipping of Compounds. All authorized shipping requests enter the shipping backlog. On a daily basis, the Storage contractor lists the shipping specifications for items in the backlog so that assembly of the shipment can begin. For each separate shipping list, material for each of the items on the list is located and retrieved from the repository, weighed out in the requested amount, and packaged for shipment. Laboratory stations fully interfaced with the DIS support these operations. After a shipping request has been packaged for shipment, a separate step provides support for the actual shipment of the material. Final shipping lists are printed for inclusion with the package.

Receipt Acknowledgment. When a shipment arrives at a screening laboratory, a DIS program is used by the screener to acknowledge that receipt. Deviations from the accompanying shipping list may be specified as necessary with the

acknowledgment. When testing of a compound has been completed, all excess material is returned to the repository by the screening laboratory, and this final shipment in the cycle is recorded in the Shipping History database. The returned sample is logged in like any other sample, and the Inventory database is modified appropriately.

It should be noted that the solid lines shown in the diagram of Figure 1 indicate the movement of chemical material from one step of the process to another. Similarly, the dashed lines indicate the transfer of information between steps. In some cases, information is transferred by means of printed reports or listings, in other cases through the updating of DIS databases, and in still others by means of both mechanisms.

The above descriptions of each of the major steps in the inventory and shipping operations have necessarily been simplified to a large extent. Additional details concerning the DIS support provided for these major steps, as well as the contingency procedures built into that support, are provided in the following sections.

RECEIPT AND REGISTRATION

As discussed in part 2 of this series,⁵ the acquisition of all material is considered to be the responsibility of a particular NCI contractor, referred to herein as the Acquisitions contractor. Orders for new compounds are automatically placed by the DIS as those compounds are selected for testing by the DIS Pre-Registry subsystem. Orders for additional material for existing compounds are manually placed as the need for such material arises. All others (both new and refills) are recorded in the DIS Order database.

As material is received at the Acquisitions contractor for various compounds, the DIS is used to record the receipt of material against an appropriate outstanding order. Provisions have also been made for the receipt of unordered material. If the amount of material received is known, that amount is entered as part of the receipt procedure; otherwise, the amount is left unknown. This material is then registered with the DIS as was explained in part 2 of this series. If the compound represents an initial acquisition, this fact is first confirmed by structural uniqueness tests, and then the compound is assigned a new NSC Number. If the receipt represents additional material for an existing compound, then a new sample number under the appropriate NSC Number is assigned to the compound. In either case, barcoded bottle labels identifying the sample are printed and affixed to the bottles. Both an initial Inventory database record and an initial Shipping History database record for the sample are created in those DIS databases. This begins the inventory/shipping process for that sample. The initial Inventory record contains information on the supplier of the sample, dates of acquisition, and amount of material received (if known). The initial record placed into the Shipping History database at this time represents the shipment of the material from the supplier to the Acquisitions contractor and records dates sent and received.

Material received at the Acquisitions contractor is generally transferred to the Storage contractor on a daily basis. To support this operation, the DIS provides a special command that will generate a "courier list" itemizing all samples which have been received since the last transfer of material to the Storage contractor. Any pertinent user hazard or safe storage notes are also included on this listing. A copy of this listing accompanies the material sent to the Storage contractor and is signed by the Storage contractor to acknowledge receipt at that site. The use of the special command also creates a second record in the Shipping History database for each sample on the list; this record represents the transfer of material from the Acquisitions contractor to the Storage contractor. Only the shipping portion of the record is filled at this time, however;

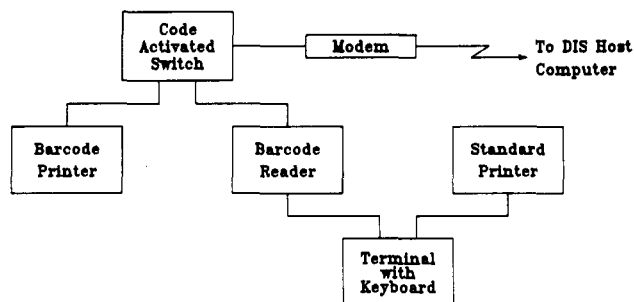


Figure 2. Storage contractor label reading/printing workstation.

the corresponding receipt portion of the record is filled when the Storage contractor indicates receipt as described below.

ENTRY OF COMPOUNDS INTO THE REPOSITORY

When material arrives at the Storage contractor, it must be logged into the repository maintained by this contractor. Most commonly, this material is that transferred from the Acquisitions contractor as described above. At other times, however, excess material is returned to the repository by the screening laboratories as is described in a separate section, below. To support both of these operations efficiently, a special label reading/printing workstation logged directly into the DIS is used. The arrangement of this workstation is shown schematically in Figure 2.

The special workstation incorporates both barcode reading and printing devices as well as a standard nonintelligent CRT terminal with keyboard and printer. The barcode reader, a hand-held wand device, is inserted between the terminal and the modem so that anything read by the wand will be transmitted to the host DEC System 10 computer as if it had been entered through the keyboard. To permit separate printing of barcode bottle labels, a code-activated switch is further inserted between the barcode reader and the modem. When a label is to be printed, this device is switched (by a special command sequence from the host computer) so that output is directed to the label printer rather than to the CRT terminal, the label is printed, and the device is switched back so that subsequent output is directed to the terminal.

To log material into the repository, this workstation is logged into the DIS and a special command is used to indicate the items received. In the case of the material transferred from the Acquisitions contractor, each sample is wanted to read the identifying information from the bottle label affixed by that contractor. Other pertinent information, such as the date of receipt, the bottle type, and the shelf location where the material is to be stored, is entered through the terminal keyboard. As this is done for each of the samples received at the repository, the DIS Inventory and Shipping History databases are updated appropriately. Receipt dates and bottle-type information are added to the Inventory database record for the sample, and the same information is added to the Shipping History database record, which represents the transfer of material from Acquisitions to Storage contractors, thus completing the transaction represented by that record.

Similar procedures are used to log the excess material returned by the screening laboratories back into the repository. Here, however, barcoded bottle labels may not be available, and the identifying information may need to be entered through the keyboard. It is also generally necessary to print a new barcoded bottle label for the storage of these items in the repository, and this is done on the barcode printer, which is a part of the workstation.

In a separate operation associated with the entry of material into the repository, the amount of material that has been received must be determined. A reliable figure may be available from another source such as the supplier, in which

case that figure can be entered by the Storage contractor. Otherwise, the contractor must weigh the sample. This is generally done with the special weigh station equipment described later, but alternatively, the weight may be measured independently and entered manually by using the label reading/printing workstation discussed in this section. In either event, the determined weight is recorded in the DIS Inventory database as the weight of the sample.

ADJUSTMENT FOR SCREENING CAPACITY

As discussed in the next section, the DIS automatically generates shipping requests for new compounds that have been received for initial testing. In order to determine to which of the multiple screening laboratories² under contract to NCI each such shipment is to be directed, the DIS maintains a record of the unused capacity of each screening laboratory for performing such tests. In the automatic procedures, the DIS only decrements these capacity figures by the numbers of compounds shipped. This precludes erroneous assumptions concerning the freeing-up of additional capacity. It does require, however, that the screening laboratory capacities be periodically reviewed and updated by NCI officials. The DIS provides a means of accepting updated capacity figures from properly authorized individuals. Any attempt to update the capacity figures by any other individual will, however, be rejected.

AUTOMATIC SHIPPING LIST GENERATION

All initial acquisitions received at the repository are normally automatically included in the shipping request to a screening laboratory where they receive their preliminary testing. The only exceptions to this rule are compounds that have been marked (flagged in the DIS Inventory database) to be held for special testing or to be held in quarantine.⁶ New compounds actually become eligible for inclusion in one of these automatic requests after they have been entered into the repository as described above so long as valid sample weights have been entered for the compounds.

Periodically, the DIS will collect all such compounds onto one or more automatically generated shipping lists. In this generation process, an analysis of the unused capacities of the various screening laboratories for performing such tests is made to identify the laboratory with the largest unused capacity (as set by the adjustment procedures discussed in the preceding section). The first such list will then be directed to that laboratory. The size of this list (number of compounds included on the list) is limited by the number of compounds available for shipment, by the unused capacity of the laboratory for performing such tests, and by a fixed maximum number, currently 36.⁷ The unused capacity of that screening laboratory is then decremented by the number of compounds on the list. If still more compounds are available for shipment following the generation of such a list, the unused capacity of the screening laboratories is again analyzed, and another list is generated to the laboratory with the next highest capacity. This process continues until no more compounds are available for shipment or until no more unused capacity remains at the screening laboratories.

Shipping lists containing less than a fixed minimum number of items (typically 10) will not be generated in this completely automatic process. The automatic generation of such small lists can, however, be manually triggered by a properly authorized individual if desired.

MANUAL SHIPPING LIST REQUESTS

As discussed in the preceding section, shipping requests for the initial testing of new compounds are generated automatically by the DIS. All other shipping requests, whether for

Shipping List: 8502706-H Date Shipped: 06-DEC-85 Date Received: 11-DEC-85

Shipment Type: Storage Contractor to a Screener

Method of Shipment: M

Requested by: N. GREENBERG (NCI/DEB)

Receiver: S03-0

Ms. Margaret A. Sheridan
Biomedical Sciences Section
Battelle Columbus Labs
505 King Avenue
Columbus, OH 43201

Cntr. No.	NSC/Sample	Amount Requested	Amount Shipped	Amount Received	Comments
1	740-K/82	1 gm	1 gm	1 gm	
2	8806-C/30	1 gm	1 gm	1 gm	
3	19893-G/10	5 gm	5 gm	5 gm	
4	26271-N/31	5 gm	5 gm	5 gm	
5	123127-R/46	1 gm	1 gm	1 gm	
6	409962-T/20	5 gm	5 gm	5 gm	
7					(a)

Cntr. No.	NSC/Sample	Systems	Test	Special Instructions	Hazard/Storage Codes
1	740-K/82	ST	POSITIVE CONTROL		ALK HTX PSN DRK
2	8806-C/30	ST	POSITIVE CONTROL		ALK
3	19893-G/10	ST	POSITIVE CONTROL		PSN PSN CRC TOX
4	26271-N/31	ST	POSITIVE CONTROL		PPD
5	123127-R/46	ST	POSITIVE CONTROL		CRC DRI RFG
6	409962-T/20	ST	REMOVED FROM SHIPMENT		ALK IRT EXP CHL FRZ
			POSITIVE CONTROL		

(a) This sample has been used to provide sufficient material for shipment.

Figure 3. Example of a shipping list to a screening laboratory.

follow-up testing of particular compounds at specific screening laboratories or for the disbursement of material to other (nonscreening laboratory) recipients, must be manually specified. Again, the DIS provides a special command to assist with the manual specification of these other types of shipping requests.

A typical shipping list in its final form is shown in Figure 3. All phases for the shipping process had been completed at the time this shipping list was printed, so that the list shows request, shipment, and receipt data. Various intermediate forms of this list containing other types of information also may be produced by the DIS, but this final form of the list illustrates all the major categories of information included on the list. Each shipping list is assigned a shipping list number by the DIS, and the one shown in Figure 3 was the 2706th request of calendar year 1985. The list contains three principal sections: (1) a header; (2) a packing list (showing amounts); and (3) an instructions list (indicating what is to be done with the material).

The DIS supports the online specification of such shipping requests by prompting for the information to be included on the list. Thus, the user is first prompted for the recipient of the shipment, and this information is entered into the list header. Screening laboratories, the major recipients of all shipments, may be identified to the DIS by means of their Namecodes. In fact, any recipient may be identified by a DIS Namecode, provided, of course, that they have an entry in the DIS Namecodes database. If the recipient has no Namecode, then the work "name" is entered in place of the Namecode. This causes the program to prompt for a name and address. When a Namecode is entered, the DIS retrieves the name and address from the Namecodes database. Likewise, the identity of the requestor is known to the DIS by virtue of the computer account being used to specify the request.

The requestor will then be prompted to specify each of the items to be included on the shipping request. Four special pieces of information are involved here: (1) the NSC/Sample Number identifying the compound and specific sample of that compound from which the material is to be drawn; (2) the amount of material to be shipped; (3) the tumor system(s) against which the material is to be tested at the screening laboratory; and (4) any special instructions to be communicated to the screening laboratory for that particular item. The first three of these pieces of information are validated by the system and are rejected if invalid. The NSC Number must be accompanied by its correct check character, and the same is true of any Namecode entered. If in either case the correct check character was not provided, the DIS refuses to proceed until the problem is rectified. When the requestor specifies

the amount of the particular NSC/Sample that is to be shipped, the DIS checks the Inventory database to determine whether the requested amount of material is available and uncommitted, i.e., not earmarked for other pending shipping requests. If sufficient uncommitted material is not available, the user is shown a list of all available material for the compound and is presented a range of alternatives including the specification of a different sample number, the modification of the requested amount, the mixing of different samples of the same compound, or the withdrawal of the request. The requestor may also indicate that the request is to proceed as specified in the hope that more material will be found in the repository than is indicated in the Inventory database. This alternative is permitted because there is known to be a considerable amount of very old and sometimes inaccurate amount data in the Inventory database.

When all items to be included on the shipping list have been specified in this manner, the DIS will display the shipping request in the general form shown in Figure 3 so that the requestor may review the shipping specifications. A full set of edit capabilities are provided to permit the modification of any of the information that may be found to be in error. When all desired modifications have been made, the requestor may then submit the request to the authorization process, described in the next section.

AUTHORIZATION OF SHIPPING LISTS

All shipping requests must be duly authorized by one or more NCI officials before shipment can proceed. In particular, all shipments to screening laboratories must be authorized by officials before shipment can proceed. In particular, all shipments to screening laboratories must be authorized by officials of two separate NCI branches because such a shipping request is implicitly a work order to two contractors, the Storage contractor and the screening laboratory. Shipments to nonscreening laboratories, however, need only be authorized by the NCI branch that manages the storage contract. The DIS supports this authorization process by making the pending shipping requests available for review by those individuals who are fully authorized to approve a shipping request for the branch with which they are associated. All requests to access this capability are fully screened by the DIS to ensure that the requestor has the proper authority to perform the authorization operation. The organizational affiliation of the requestor is also checked to ensure that they are a member of the appropriate branch.

For properly authorized individuals, the DIS can support the authorization of shipping lists in a fully interactive manner. In this mode, the shipping requests are displayed on the user's terminal in the form of a shipping list similar to that shown in Figure 3, and the user is given an opportunity to approve the request as it stands, to modify and then approve the request, or to reject the request. Authorization can also be done in a batch-assisted mode in which lists of the pending requests are printed for the authorizing individuals on an overnight basis, and the authorizer then need only indicate the shipping list numbers of those lists to be authorized. Again, lists can be modified or rejected if desired.

In the case where two separate individuals must authorize a shipping request, the DIS will maintain the request in a pending status until both have done so. If one of these individuals should modify the request, any previous authorization of the list by the other individual will be erased and the list will again be displayed for authorization to that individual with all changes highlighted. Only when both individuals have approved an identical form of the request will the request be considered, from the contractual point of view, to be authorized.

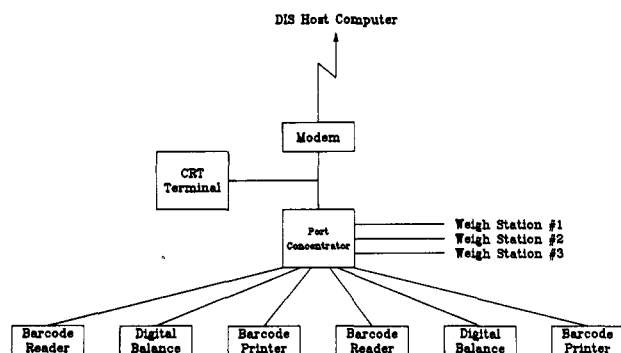


Figure 4. Storage contractor laboratory weigh stations.

BACKLOG REVIEW

When shipping requests have been fully authorized, those shipments may then be prepared and shipped by the Storage contractor. The Storage contractor, who is logged into the DIS on essentially a continuous basis, using the workstation shown in Figure 2, reviews the shipping backlog at regular intervals. In such a review, a record of each of the newly authorized shipping requests will then be printed on the standard printer attached to that workstation. These will be printed in shipping list form, similar to the example of Figure 3, but will also show shelf location of the requested material in the repository rather than the testing instructions shown in that example. At the same time, barcoded labels will be printed for the shipping list and for each item on the shipping list that is not already so labeled in the repository.⁸

This information is then used by Storage contractor personnel in the preparation of the shipment. The shipping list label is attached to the printed copy of the shipping request, and the bottle labels are saved for attachment to the bottles from which the shipped material is to be drawn.

SHIPMENT PREPARATION

To prepare a shipment, the Storage contractor uses the printed copy of the shipping request to withdraw all necessary material from the repository shelves. Barcoded labels are also attached at that time to any bottles that do not already have such labels. The bottles are then taken to one of the laboratory weigh stations located in exhaust hoods, where the requested amount of material can be parceled out for shipment.

The laboratory weigh stations are interfaced to the DIS by the equipment illustrated schematically in Figure 4 so that the parceling operation can be done while online to the DIS. In this manner, the DIS Inventory database can be updated directly as a result of the weigh operation and need not be updated by means of a separate operation at a later time. As with the weighing operation described above, an alternative means of manually specifying the parceled weights is provided by using the label reading/printing workstation, but this is not the preferred method of performing this operation and is, in fact, discouraged because it offers only limited control over the integrity of the data entry.

As can be seen in the schematic of Figure 4, each of the five laboratory weigh stations has a barcode reader and a digital balance. Two barcode printers are shared among the five weigh stations. All of this equipment is interfaced to the DIS on the host computer by means of a port concentrator, enabling all communication to the host to be accomplished over a single telephone line. A standard nonintelligent CRT terminal is used to log the system into the DIS and to display certain types of auxiliary information concerning the communications process.

The barcode readers used at these weigh stations have a one-line display that allows prompts to be issued by the DIS

to the station operator. In response to these prompts, the station operator may wand commands from preprinted menus, may wand identifying information from bottle labels, or may weigh material on the digital balance. For example, to weigh out the material to be shipped to satisfy a particular request, the operator first wands the command for performing this operation from a preprinted menu. In response to a prompt issued by the DIS, the operator next wands the shipping list label from the printed copy of the shipping request. The operator then begins weighing out the items on that shipping list. For each, identifying information is wanded from the bottle label. The requested amount of material is then parceled into a separate bottle on the digital balance and, when that is done, a foot switch on the balance is pressed by the operator to record the amount of material parceled into the separate bottle. This entire operation can be completed without the operator having to type anything, and indeed, the weigh stations are not equipped with keyboards.

The operator proceeds in this manner with all of the items on the shipping list. For any for which material cannot be found, no action need be taken by the operator. For any for which material from a different sample is substituted—either partially or fully—special commands that can be wanded by the operator permit this to be specified to the system. The outcome of such a change can be seen in Figure 3, where sample number 15 was used to fill container 6. Provisions are also made for cases where multiple bottles of the same sample must be used to obtain the requested amount of material.

As each of the items on the request list is weighed, the amount in the DIS Inventory database for that sample is decremented by the weighed amount. Thus the DIS Inventory database generally contains a completely up-to-date record of the amount of material remaining in each sample.

SHIPMENT OF SAMPLES

When a shipment has been prepared in the manner described in the preceding section, the material to be shipped is packaged for shipment and the DIS is used one final time to finalize and record the shipment. This is done from the label reading/printing workstation (see Figure 2), where a keyboard is available to interact with the system as necessary. The shipping request list used to prepare the shipment, together with annotations made on that list concerning deviations from the request, is used in this final shipping operation.

To finalize a shipment, that shipment is called up by means of the shipping list number. The DIS will immediately compare the amounts parceled out for each item on the list vs. the requested amounts. Where these deviate by more than 5%, the person finalizing the list will be asked to enter a reason for the deviation. Any other pertinent comments concerning the actual amounts shipped may also be entered at this time. When all available information of this type has been entered, the list can be either finalized or deferred for the entry of still more information at a later time.

When the list is finalized, several things occur. First, final copies of the shipping list are printed on the standard printer associated with the workstation. One of these copies is packed with the shipment. Second, the shipping list is added to the DIS Shipping History database and becomes immediately available for displays of shipping lists associated with all compounds on the list. Finally, electronic messages concerning any discrepancies between requested and shipped amounts are automatically sent to the NCI staff who had originally requested the shipments.

The final copies of the shipping list are in the form shown in Figure 3, except that the "Amount Received" column is, of course, not included on the list. Note that in the example shown in Figure 3 no shipment was made for container number

6. Rather, material from sample number 15 of the same compound was substituted. The Storage contractor has authority to do this when sufficient material is not available in the specified sample.

ACKNOWLEDGMENT OF SAMPLE RECEIPT

As indicated in previous discussions, shipments of material are made both to screening laboratories and to other designated recipients. Since the screening laboratories are directly affiliated with the DTP project, they are required to log into the DIS and acknowledge receipt of all shipments. There is no such requirement for other recipients of shipments, and thus the receipt-acknowledgment phase of the shipping operations applies only to shipments to screening laboratories.

When a screening laboratory signs into the DIS to acknowledge receipt of a shipment, the received shipment is indicated by shipping list number. If all material has been received as specified on the shipping list packages with the shipment, that is all that needs to be done. If, however, there is some deviation between the amount received and the amount shipped (due to breakage, for example), then this must be indicated to the system. The container numbers of the items in question are entered along with a received amount (usually approximate) and a reason for the discrepancy (breakage, etc.). This information is used by the DIS to update the shipping list stored in the Shipping History database. Amounts received are placed into that column of the list, and any discrepancy reasons are placed into the comments column of the list. The receipt-acknowledgment phase of the operation completes the shipping process for any given shipment.

SAMPLE RETURNS

When a screening laboratory has completed all specified tests on a sample, any excess material is normally returned to the repository maintained by the Storage contractor. This is done by simply packaging that material and shipping it to the Storage contractor. No records of such shipments are entered into the DIS at that time. Rather, when the returned materials arrive at the Storage contractor, they are logged into the repository as described earlier. This operation both updates the DIS Inventory database to include the returned amounts and includes a record of the return transaction in the Shipping History database.

TRANSSHIPMENT OF SAMPLES

When a compound shows activity in its preliminary testing, NCI policy, described in part 5 of this series of papers, requires that confirmation of this activity be sought in an independent screening laboratory. As a result, it frequently transpires in such cases that a sample needs to be shipped from one screening laboratory to another. This process has been designated "transshipment" and is supported by the DIS in the following way. Properly authorized NCI individuals may specify a transshipment in much the same manner in which regular shipments to screening laboratories are requested. Thus, all of the items to be shipped, the amounts to be shipped, and the testing instructions for the recipient laboratory are entered into a shipping list. The only difference in the information included on the list is that the shipping laboratory, rather than the storage contractor, is identified on the list header.

When a transshipment list has been specified in this manner, three copies of the list are generated by the DIS. Two of these copies are sent electronically to the two screening laboratories by means of a DIS logon message, i.e., when someone at the screening laboratory next logs into the DIS, the shipping list will be printed on their terminal. The third copy of the list is printed offline by the DIS and returned to the requestor at

NCI as a record of the request.

When the first screening laboratory receives the shipping request via the logon message, the shipment is prepared and sent to the second screening laboratory. When that laboratory in turn receives the shipment, a standard DIS receipt acknowledgment operation is used to indicate receipt of the shipment. Shipping lists associated with these transactions are entered in the normal manner into the Shipping History database. These shipments do not, however, impact the Inventory database since material stored in the repository is not affected.

DIRECT SHIPMENTS

An irregular procedure which will not be found in the schematic of Figure 1 is that of direct shipments from the supplier of a chemical to the screening laboratory where the chemical is to be tested. Such samples are never sent to the Acquisitions contractor, nor are they entered into the repository maintained by the Storage contractor.⁹

In these cases, compounds are still selected for testing in the normal manner outlined in part 2 of this series of papers, but following the Pre-Registry processing, the DIS sends letters to the suppliers asking them to ship the material directly to the screening laboratory. When the material is subsequently received at the laboratory, the receipt is indicated to the Acquisitions contractor who logs the material into the DIS in the normal way as a new compound or as an additional sample of an existing compound but indicates that the material was sent directly from the supplier to the screening laboratory.

For new compounds received in this manner, the DIS will automatically include those new compounds on a shipping list directed to the screening laboratory, and the list constitutes an authorization for the laboratory to perform initial tests on those compounds. This is done in much the same manner in which new compounds received at the repository are automatically included on shipping lists, which has already been described. For additional samples of existing compounds received in this manner, shipping lists (which carry testing instructions) must be generated in a manual procedure very similar to that used to generate shipping requests for compounds in the repository. Thus, the particular chemicals to be tested and the testing instructions are specified in shipping list form by the requestor.

When these direct shipment testing requests have been generated, either automatically or manually, they are entered by the DIS into the backlog of pending shipping requests. Thus these requests will be presented for authorization to the appropriate NCI individual¹⁰ in the normal manner. Following the authorization step, the DIS will print copies of all such direct shipment lists for mailing to the screening laboratory. No acknowledgment of the receipt of these lists is required of the recipient laboratory.¹¹

INVENTORY DATABASE

As indicated throughout the previous discussion, the DIS Inventory database is an integral part of the Inventory/Shipping package. This database is accessed frequently during the course of the inventory and shipping operations and is also updated at appropriate points in those operations. As pointed out in the first of this series of papers, all information included in the DIS databases can be displayed on request by appropriately authorized DIS users, and much of that information can be searched. A record exists in the Inventory database in association with each sample of each compound that has been subjected to the *in vivo* testing procedures. The major types of information included in this database are as follows: identification information such as NSC/Sample Numbers and compound names and lot names provided by the supplier;

acquisition information such as supplier identification, dates of acquisition, and submission category codes; repository information such as amount in stock, amount uncommitted to other pending shipping requests, amounts in individual bottles, bottle type, and shelf location; other information such as melting points and boiling points, physical state, quarantine and hold for special testing flags, confidentiality flag, and miscellaneous comments.

SHIPPING HISTORY DATABASE

The DIS Shipping History database is also an integral part of the DIS Inventory/Shipping package and can be accessed and updated in the same manner as the Inventory database. This database contains a record for each shipping transaction made against a particular sample of a particular compound. These transactions begin with the shipment of material from the supplier to the Acquisitions contractor and continue with each movement of the sample, or a portion thereof, from one location to another. A record is also inserted in the Shipping History database whenever a sample is reweighed by the Storage contractor. Thus the Shipping History database provides a complete audit trail of the material received for a sample; it shows the amount originally received, the amounts shipped to various screening laboratories for testing and to other nonscreener recipients, and adjustments made to the amount on hand in any reweigh operations performed by the Storage contractor. The major types of information included in each record in the Shipping History database are as follows: identification information such as NSC/Sample Number and shipping list number; type of shipment information such as supplier to Acquisition contractor, Storage contractor to screener, Storage contractor to nonscreener, etc.; requestor information such as identification, amount and date requested, and test instructions; sender information such as identification, amount and date sent, and method of shipment; recipient information such as identification and amount and date received.

SUMMARY

The DIS Inventory/Shipping package has been designed to support the frequent shipment of small amounts of material from a large repository of chemical compounds. This is characteristic of the NCI screening project, where an inventory of several hundred thousand different chemical compounds, many of which have multiple samples, is maintained and from which shipments are made both to screening laboratories for anticancer testing and to other requestors of the compounds. Approximately 300 shipments per month are made from this repository, each containing from 1 to 36 different chemicals.

Two major databases within the DIS support these activities. These are the Inventory and Shipping History databases. The Inventory database records the current status of the repository for any given chemical, while the Shipping History database maintains an audit trail of the disposition of chemical material. A considerable amount of special software supports the in-

ventory and shipping operations of the project, while at the same time accessing and updating those databases as necessary. Barcode reading and printing equipment as well as digital balance equipment is automatically interfaced to this software to further improve the efficiency of capturing the inventory and shipping data.

This Inventory/Shipping package of the DIS has been in operational use by NCI and associated contractors since March 1985. The use of the systems has improved the efficiency of the inventory and shipping operations by a significant factor. Even more important, perhaps, is the fact that the system has ensured that all necessary information associated with these operations is recorded and is available for recall by means of relatively simple search and display requests whenever needed.

REFERENCES AND NOTES

- (1) The Acquisitions contractor is not equipped to handle hazardous substances and is therefore instructed not to weigh samples that are received. When the sample weight is provided by the supplier, it can be entered and flagged as "estimated".
- (2) The screening laboratories that are currently under contract to NCI are The Southern Research Institute (Birmingham, AL), Battelle Columbus Labs (Columbus, OH), Illinois Institute of Technology Research Institute (Chicago, IL), Mason Research Institute (Worcester, MA), Institut Jules Bordet (Brussels, Belgium), Arizona State University (Tucson, AZ), and the University of California (Los Angeles, CA).
- (3) The NCI screening program has always been international in character, soliciting chemicals for testing from organizations all over the world. In keeping with this, requests for samples of the chemicals in the NCI repository are accepted from any qualified investigator. Such requests are always honored provided that material is available and that its distribution is not precluded by confidentiality considerations.
- (4) A variety of flags can be assigned to a compound and will prevent the DIS from automatically shipping a compound to screeners. The most important of these is a "hold" flag, which requires that the DIS postpone shipment until a specific NCI employee approves.
- (5) Milne, G. W. A.; Feldman, A.; Miller, J. A.; Daly, G. P.; Hammel, M. J. "The NCI Drug Information System. 2. The DIS Pre-Registry". *J. Chem. Inf. Comput. Sci.* second of six papers in this issue.
- (6) Compounds are "quarantined" when it is necessary to control an entire sample. The most common instance of this is when a compound has been selected for possible clinical trial. An "Investigational New Drug Application" (INDA) permitting such trials must be submitted to the Food and Drug Administration (FDA). The FDA requires that all data submitted in an INDA be collected under Good Manufacturing Practices. Accordingly, a large sample of the compound is synthesized for NCI and sent to the Storage contractor, where it is quarantined pending the completion of an independent purity analysis.
- (7) This number has been used for a number of years because it results in an optimally sized package and is also a convenient number from the point of view of the screening laboratories.
- (8) Only bottles added to the repository since the inception of the DIS in March 1984 are barcode labeled. During the shipping activity, bar-coded labels are printed for those repository bottles that are accessed and found to have no bar-coded labels. The new labels are necessary in the sample weighing step.
- (9) Direct shipments occur primarily in Europe where various long-lived three-way relationships exist between NCI, a supplier, and a screening laboratory. Few, if any, parallel situations are to be found any longer in the U.S.
- (10) In these cases, because the Storage contractor is uninvolved, only a single authorization, directed to the screening contractor, is required.
- (11) Prior to January 1986, computer network access to the NIH computer center was not supported, and as a result, a number of compromises were built into the DIS, particularly in regard to European operations. Now that network access is possible, it is expected that improved transatlantic communications will allow some of the anomalies to be resolved.