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A COMPUTER BASED LABEL-PRINTING SYSTEM FOR CLINICAL TRIALS SUPPLIES

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INTRODUCTION

The packaging of clinical trial supplies is a critical phase of drug development. The labelling of such studies can become difficult due to the use of identical active, placebo and reference drugs with complicated treatment schedules. The labels need to show patient numbers together with treatment periods. Traditional printing machines can change numbers automatically but cannot sort labels destined for different products ready for packing. This stage is both very time consuming and presents one of the greatest risks of error in the packing operation. We therefore decided to develop a computer-based system which would contain rapid, error-

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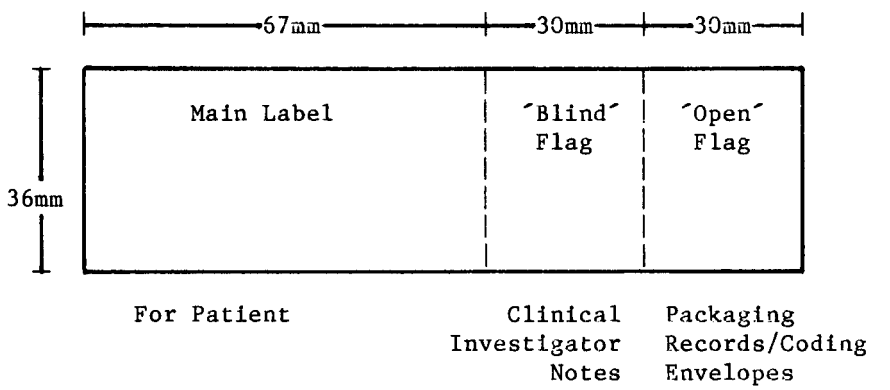
free printing in an adaptable format with automatic archiving and other GMP/GCP* advantages.

LABELS

A self-adhesive three-part label was selected (figure 1). All three sections carry the information needed to identify the individual treatment - trial code, patient number, treatment number. The main part of the label carries information for the patient (company details, dosage, expiry etc...). Company details are generally preprinted since this is clear even in very small typefaces, and because some countries require coloured warning statements. There are two small detachable flag sections. In addition to the treatment identification, one "open" flag carries the

FIGURE 1 : THREE-PART SELF ADHESIVE LABELS



* GMP stands for Good Manufacturing Practice.
GCP stands for Good Clinical Practice.

name of the drug treatment. This is used as a control in the packaging operation and we consider this a major aid to GMP in our laboratories. It is removed during packaging and can subsequently be used to prepare emergency decoding envelopes for the clinical investigator. The central "blind" flag carries only treatment identification and remains attached to the container with its backing paper. It is detached by the clinical investigator and fixed to the patients' notes allowing verification of the drugs supplied.

EQUIPMENT

Labels are printed on a Decwriter III LA120 console printer (Digital Equipment Corporation) which also serves as a general-purpose printer. The variable line-spacing facility of this machine is used to slightly separate the first "title" line from the rest of the text and to ensure that the text fits neatly on the labels which do not correspond to a whole number of lines. The variable character size option is used to print the patient number in large numerals to aid rapid identification. (The number is also overprinted to increase contrast). It would be possible to develop the system with this printer to mix character sizes on one label.

The printer is used in conjunction with a PDP 11/70 computer (Digital) running under the UNIX(TM) operating system (Bell Laboratories). The programme is written in "C" and is terminal dependent. The executable code is 26 Kbytes. Data can be entered

on a conventional VDU and a special command suppresses the terminal dependant parts of the programme.

DATA ENTRY

In order to set up a label-printing run, three files are created containing the text, trial design and randomisation. This allows great flexibility of usage. For example, in a multicentre trial, different texts may be used with a common design file and different parts of a large randomisation. A sample label is shown in figure 2.

Text File

The text file contains :

1. The number of lines (8 for blank labels, 6 for preprinted excluding trial identification).
2. The title for patient (e.g. Patient, Volunteer) used on the flag labels.
3. The title for patient used on the main label, which may be abbreviated to save space (e.g. Pat.).
4. The title for the treatment period (e.g. Week, Bottle) used on the flag label.
5. The title for the treatment period used on the main label.
6. The text.
7. The trial code.

On the main label the trial code, treatment period and patient number are always printed as the last line (the appropriate period and patient numbers being captured from the design and ran-

FIGURE 2 : SPECIMEN LABEL

LERS - Synthelabo 58, rue de la Glaciere, Paris ANTIHYPERTENSIVE TRIAL Take one tablet every morning Use before Jan. 1985 Trial 123 Weeks 1&2 Pat.99	PATIENT 99 WEEKS 1&2 Trial 123	PATIENT 99 WEEKS 1&2 Trial 123 BETAXOLOL 20mg

domisation files). The code is automatically repeated on all three sections.

Design File

The design file contains :

1. The number of drugs.
2. The names of the drugs (used on the flag label).
3. The number of groups of patients.
4. The number of labels per patient (that is, the number of treatment periods).
5. For each group of patients and for each treatment period, the drug to be taken, coded by the number given in section 2.
6. The names of the treatment period (if the first treatment period is "weeks 1&2" and the second "weeks 3&4" the title entered in the text file is "weeks" and the names entered in the design file are "1&2" and "3&4").

A specimen file is shown in figure 3 which represents the summary printed by the programme and not the way in which data is entered.

FIGURE 3 : SPECIMEN DESIGN FILE

Number of drugs : 5
Number of Patient Groups : 4
Number of labels per Patient : 7

Drug 1 : PLACEBO
Drug 2 : BETAXOLOL 20mg
Drug 3 : BETAXOLOL 40mg
Drug 4 : ATENOLOL 100mg
Drug 5 : ATENOLOL 200mg

	Drug Number				Name of Treatment
Group	1	2	3	4	Period
Label 1:	1	1	1	1	1
Label 2:	2	2	4	4	2&3
Label 3:	2	3	4	5	4&5
Label 4:	1	1	1	1	6
Label 5:	4	4	2	2	7&8
Label 6:	4	5	2	3	9&10
Label 7:	1	1	1	1	11

This file is for a double-blind, cross-over evaluation of Betaxolol 20mg and Atenolol 100mg with each group splitting during treatment to continue with the same dose or to take double the dose. There are one week placebo washouts before, between and after active treatments, which are four weeks long (2 weeks original dose, 2 weeks original or double dose). All five products are identical.

Randomisation File

This file contains :

1. The number of groups of patients.
2. The number of patients in each group (groups may be unequal in size).
3. The actual randomisation.

The randomisation may be entered in two ways, to minimise the risk of errors in transposing onto the computer data from protocols written in different styles.

a. For each patient in turn the group to whom that patient belongs may be specified by number, as defined in the design file.

b. For each group in turn the appropriate patient numbers may be given.

Randomisations which contain the same patient twice, which do not contain consecutive patient numbers or where the wrong number of patients appears in a group are rejected by the programme which then provides editing facilities to correct the errors.

An option allows letters to be used in place of numbers which is useful in some complex studies.

ARCHIVING

All data files are automatically archived. The trial code numbers are used as file names for ease of reference. Files may be "locked" to prevent unauthorised or accidental changes. The printer will also produce hardcopies if required for manual archiving. Old files are transferred to magnetic tape, but all current data is immediately accessible on disc. It is possible to record label production for reconciliation purposes.

PRINTING

To print labels it is necessary to specify the three files to be used. The patient number(s) and/or treatment period(s) may be specified if all labels are not required. The programme then as-

sembles the required text together with the period and drug names (from the design file) and patient numbers (from the randomisation file). Labels are derandomised (i.e. sorted by drug name) for printing.

Any part of the label can be omitted by leaving the appropriate section of the file blank or by selecting the un-numbered label option. (Dummy design and randomisation files are available for producing identical labels).

USER ENVIRONMENT

The programme was developed for ease of operation and is readily mastered by non-technical staff. The programme is interactive. Many questions need no response in normal use, the programme defaulting to the most commonly required reply. For example, once a file name has been given, any request for a file name that receives no response defaults to the file previously named.

Data entry can be done "de novo" or by editing existing files, either to correct errors or because the file needed is similar to an existing file. If the existing file is "locked", overwriting is not allowed.

A hierarchy of passwords allows differential permissions for staff of varying responsibilities.

Password (1)	Printing only.
Passwords (1) and (2)	Data entry.
Passwords (1), (2) and (3)	"Locking" and "unlocking" files.

CONCLUSIONS

We have developed a rapid, adaptable easy-to-use system to print labels for clinical trial packaging based on a computer printer. The sorting of labels by drug name, and the use of an "open" flag label carrying this name saves much time and is of major importance in reducing the risk of labelling errors. The use of a "blind" flag label for the clinical investigator's notes facilitates the clinical monitors task. The automatic archiving and rapid access to exact details of labels printed is also valuable.