BLINDING OF INVESTIGATIONAL PRODUCTS

PART OF THE CLINICAL SUPPLY KNOWLEDGE SHARE SERIES
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THE NATURE OF CLINICAL PRODUCTS UNDER DEVELOPMENT IS CHANGING. WITH THE RISE OF TARGETED THERAPIES AND THE INCREASING NUMBER OF ONCOLOGY CLINICAL TRIALS, BIOLOGICS ARE AN EVER INCREASING PROPORTION OF INVESTIGATIONAL PRODUCTS.

44%

The ratio of small to large molecules in development is reaching an almost even split with 44% OF NEW MOLECULES APPROVED IN 2014 BEING INJECTABLE IN DOSAGE FORM. This poses challenges for clinical supply professionals – who continually need to provide blinded supplies for clinical programmes.

THE DEFINITION OF BLINDING

Blinding or masking is intended to limit the occurrence of conscious and unconscious bias in the conduct and interpretation of a clinical trial, arising from the influence that the knowledge of treatment may have on the recruitment and allocation of subjects, their subsequent care, the attitudes of subjects to the treatments, the assessment of end-points, the handling of withdraws, the exclusion of data from analysis, and so on.

WHEN YOU APPLY THE NEED TO PROVIDE BLINDED SUPPLIES OVER THE CHANGING NATURE OF DOSAGE FORMATS, THE CHALLENGES INCREASE.
WHAT ARE THE BENEFITS OF BLINDING PATIENTS AND INVESTIGATORS?

PATIENTS
- Less likely to have biased psychological or physical responses to intervention
- Less likely to seek additional adjunct interventions
- Less likely to leave trial without providing outcome data, leading to lost follow-up

INVESTIGATORS
- Less likely to transfer their inclinations or attitudes to participants
- Less likely to differentially administer co-interventions
- Less likely to differentially adjust dose
- Less likely to differentially withdraw participants
- Less likely to differentially encourage or discourage participants to continue trial

GOALS OF BLINDING
Prevent or minimize the risk of patients’ ability to differentiate between products due to the following factors:
SHAPE, SIZE, COLOUR, TEXTURE, WEIGHT, TASTE, SMELL, RATTLING, (ENCAPSULATED PRODUCT), PACKAGING
COMMON TRIAL DESIGNS

Trials generally fall into one of the following four categories:

- **Open**: Patient isn’t aware of what drug is being taken.
- **Single-Blind**: Investigator isn’t aware of what drug is being taken.
- **Double-Blind**: Both patient and investigator aren’t aware of what drug is being taken.
- **Double-Blind**: Investigator isn’t aware of what drug is being taken.

We’ll be covering RANDOMISATION and PLACEBO CONTROL in upcoming eBooks.
BLINDING METHODS

DRUG ENCAPSULATION

Encapsulation is the process of masking the test drug with the use of generic casing and fillings to prevent any detection, generally used to mask Innovator/Comparator tablets or capsules.

PACK MATCHING

The usual method of preparing blinded supplies is to remove active comparator from commercial packaging and ‘blind’ prior to repacking.

But this is not always possible...

If original packaging conditions cannot be met (e.g. sterile fill)

If sponsor lacks stability data for unpacking/repacking process

If original packaging is essential to the operation of the product (e.g. inhalers)

If matching components cannot be obtained on the market (e.g. inhaler parts, syringes)

Pack matching is based on producing placebo packs that match commercial active packs, enabling a double-dummy design to be used

Some dosage forms, such as inhalation devices, can be blinded using innovative technology and processes.
BLINDING METHODS

INHALERS – METERED DOSE INHALERS AND DRY POWDER INHALERS

BLINDING OF MDIs

- Over-embossing neutral markings onto actuators and dust caps with embossed commercial markings (e.g., brand name, logo)
- Obscuring active / placebo canister bases to hide printed / embossed lot numbers
- Sponsor sourcing of placebo canisters

CONVERSION TECHNOLOGY FOR DPIs

INHALATION PRODUCTS POSE SPECIFIC CHALLENGES. THESE REQUIRE UNIQUE BLINDING PROCESSES AND TECHNOLOGY OFTEN COMBINED WITH ANALYTICAL METHODOLOGY FOR VERIFICATION.

DOUBLE-DUMMY DESIGN

TECHNOLOGY DEPLOYED TO PRODUCE PLACEBO DPIs AT CLINICAL TRIAL SCALE:

- Disassemble units and remove active blisters without damage
- Produce placebo blister strip replicating API blister
- Accurately dosing placebo powder into blisters
- Reproducible reassembly
OTHER DOSAGE FORMS

CONSIDERATION CHECKLISTS

INHALER DEVICES
- Unit conversion
- Dismantling of filled unit
- Foil matching placebo
- Component wash
- Component reassembly
- Secondary packaging
- Pouching
- Labelling
- Canister pressure
- Sound
- Taste
- Potential residue
- Lathing of embossed print
- Dismantling of unit
- Remove all product labels
- Printed blisters/embossed

POUCHES
- Size, shape and colour
- Ink jet codes
- Tear notch

TUBES
- Ink jet/embossed codes
- Crimp thickness
- Cap styles

LABEL GENERATION
- Label stock
- Label adhesive – consideration to unit being labelled
- Transparency – critical if over-labelling
- Label backing / back numbering
- Colouration between stock
- Font style / font size
- Print boldness
- Print indentation
- Stray print marks
- No difference
- Between groups

SYRINGES
- Disassembly of components
- Safety devices
- Needle gauge
- Plunger style, length, colour
- Stopper
- Finger flange
- Product fill colour
- Barrel style
- Removal/covering of product labels

VIALS
- Primary container
- Size, shape, cap colour
- Product fill colour
- Product labelling
- Codes
- Storage conditions

REMOVAL OF EMBOSsing
- Knurl pattern to remove text on blisters

OUR BLINDING SOLUTIONS IN ACTION
VIEW OUR CASE STUDY

SHARE ME

07
ALMAC’S APPROACH TO BLINDING

HOW DOES ALMAC ACHIEVE THIS?
Ensure that the appropriate blind level is achieved and maintained.

• Processes and procedures are designed to achieve and maintain study blind within the following components:
  • Clinical supplies must not divulge their true treatment group.
  • Project documentation must be disseminated to appropriate stakeholders.
  • Business communications must not divulge unblinded information to blinded sponsor personnel.

SUMMARY
Clinical supplies are now much more varied in dosage format and require specialist blinding expertise.

• Important to remember that blinding only refers to the physical properties of the product.
• The blind may well be broken once the patient starts to use the product.
• Some drugs will produce very specific side effects – either physiological, psychological or both.
• Such side effects are impossible to match in the placebo or comparator products.

WANT MORE DETAIL?
IF YOU HAVE A SPECIFIC BLINDING CHALLENGE – TALK TO US!
ALMAC PROVIDES A UNIQUE COMBINATION OF BLINDING TECHNOLOGY AND EXPERIENCE.

COMPATIBLE WITH:
- Inhaler capabilities
- Encapsulation capabilities
- Comparator/commercial drug procurement
BLINDING OF INVESTIGATIONAL PRODUCTS

Almac Group
working together with Pharma and Biotech
to build a better global clinical supply chain

- Clinical supply chain management
- Comparator sourcing and blinding
- Global distribution
- QP release and analytical services
- Clinical supply packaging and labelling

Find out more about us at almacgroup.com