the storage location and conditions of the solution, the amount made, and the number of the batch.

5. The resulting solution will need an **identifying number** and there will be documentation associated with assigning this number.
6. The solution will need a **distinguishing label.**
7. If the solution is split into more than one container, **documented ID numbers** will need to be assigned to each container referring back to the original solution. Each container will need a **distinguishing label.**

B. Laboratory Notebooks

i. Laboratory Notebooks: Functions and Requirements

Laboratory notebooks *are assigned to individuals and are a chronological log of everything that individual does and observes in the laboratory.* Of all the documents that are described in this chapter, the laboratory notebook is the most important in research laboratories.

Laboratory notebooks in a biotechnology company are generally distributed to individual investigators by a company representative. The notebook, and the ideas and information recorded in it, are intellectual property that belongs to the company. The ownership rules in academic research institutions vary.

The primary user of a laboratory notebook is the researcher who uses the notebook to track the progress of a project, archive the data generated in experiments, record observations, and record all the details that must be remembered. Researchers use their notebooks as a key tool for trouble-shooting when problems arise.

A laboratory notebook is an important legal document that may be viewed by people in addition to the researcher. A laboratory notebook may provide evidence that is used by the scientific community to assign credit for a research discovery. The notebook documents the honesty and integrity of data that are published in research journals and used in grant applications. Laboratory notebooks can be subpoenaed in litigations and they can be examined by auditors from the FDA, EPA, and other regulatory agencies.

Laboratory notebooks are of particular importance in patent law (see Chapter 2). Laboratory notebooks are the primary evidence by which researchers prove that

Table 6.2. Types of Documentation

Examples of Documents That Are Common in Laboratories

Directive Documents

1. ***Standard Operating Procedures (SOPs)*** detail what is to be done to complete a specific task and how to document that the task was done correctly.
2. ***Protocols*** are similar to SOPs in that they explain how to do a task. The term *protocol,* however, is often reserved for situations where a question or hypothesis is to be investigated (an experiment will be performed) or the procedure is going to be performed only once.
3. ***Numbering systems*** are used to keep track of materials, equipment, and products.
4. ***Labels*** are attached to solutions, products, or items to identify them.

Data Collection Documents

5. ***Laboratory notebooks*** are a chronological log of everything that an individual does in a laboratory.
6. ***Forms*** contain blanks that are filled out by an analyst to record information. Forms are typically associated with SOPs or other documents.
7. ***Reports*** are documents generated during the execution of a protocol.
8. ***Equipment/Instrument logbooks*** keep track of maintenance, calibration, and problems for a given instrument or piece of equipment.
9. ***Analytical laboratory documents*** record information regarding the testing of a sample.
10. ***Recordings from instruments.***
11. ***Chain of custody forms*** are used to trace the movement of a sample throughout a facility and to keep samples and sample test results from being confused with one another.
12. ***Training reports*** document that individuals were properly trained to perform particular tasks.
13. ***Electronic documents*** are explained later in this chapter.

Examples of Documents That Are Specific to Production Facilities

1. ***Batch records*** are collections of documents associated with a particular batch of a product. (A batch record is both a directive and data collection document.)
2. ***Regulatory submissions*** are forms filled out and sent to regulatory agencies to inform them of what a company is doing and/or to ask permission to test or sell a product. (These are a type of commitment document.)
3. ***Release of final product record*** is filled out when a product has been approved for sale. (This is a type of data collection document.)

y were the first to conceive of an invention and in which they document the steps they took to reduce it to practice. Even academic scientists who do not seek commercial gain from their research may find that they want to patent an invention to protect their rights to it, or to ensure that their invention will remain in the public domain. It is therefore essential that all researchers maintain proper laboratory notebooks and that these notebooks unequivocally document the dates at which ideas were conceived and experiments were performed.

There are certain fundamental requirements for keeping a laboratory notebook that allow it to be used for all the purposes described above. These include:

- The laboratory notebook must be complete so that any experiment can be repeated by the researcher or someone else.
- Laboratory notebooks must be chronological to clearly document dates when events occur or ideas are conceived.
- The data in the laboratory notebook must be honestly recorded at the time they are observed.
- Laboratory notebooks should be kept in a manner that makes alterations readily apparent.

Table 6.3 contains standard guidelines that should ays be followed to ensure that a laboratory notebook meets these bulleted requirements. Laboratory notebooks are bound, for example, so that pages cannot be added or removed. This helps to ensure that the dates are correct and that the notebook honestly records what happened and when it happened. Every entry in a notebook must be made with a pen that cannot be erased, again to ensure the honesty and the integrity of the data. Mistakes are crossed out with a single line, signed, and dated. This helps ensure that entries are not obscured, altered, or changed at a later date.

ii. The Content of Laboratory Notebooks

Table 6.4 summarizes the items that are generally recorded in a laboratory notebook. All notebooks include basic information, such as the name of the person to whom the notebook was assigned and a page number and date on every page. A laboratory notebook must be complete enough that the researcher or another individual could exactly repeat the work described based on the information recorded. It is essential that laboratory notebooks include raw data. **Raw data** *are the first records of an original observation.* Depending on the situation, raw data may be written into the notebook with pen by the operator, may be a paper output from an instrument, or, increasingly, may be recorded into a computer medium (discussed later in this chapter). The researcher must save all raw data, ensure that these data are never altered or edited, and ensure that they are retrievable.

Laboratory notebook entries should include ideas as well as experiments. Researchers should explain why each experiment is performed and at the end summarize what the results show, avoiding derogatory comments about their work or ideas (even if something did not go as planned). Documenting ideas is particularly important where patents are potentially involved because the date of conception of an invention is important. Inventors need to have evidence of the date when they first had an idea and they need to show how their experiments and activities were designed to reduce the idea to practice.

One of the challenges in keeping a good laboratory notebook is that it must record clearly what actually

Table 6.3. GUIDELINES FOR KEEPING A LABORATORY NOTEBOOK

1. ***Use only a bound notebook, not a spiral or looseleaf notebook from which pages can be removed or into which pages can be inserted.***
2. ***Make sure every page is numbered consecutively before using the notebook.***
3. ***Never rip out a page.***
4. ***Keep the laboratory notebook in chronological order.*** Never skip a page to insert information later.
5. ***Blank lines or unused portions of the page should be crossed out with a diagonal line so nothing may be added to the page at a later date.***
6. ***Make all entries with indelible ink.***
7. ***Be legible, clear, and complete in your entries.*** Remember that you, supervisors, colleagues, patent attorneys, and regulatory agency inspectors may review your entries.
8. ***Enter all observations and data directly into the notebook—not onto a paper towel or the back of your hand.***
9. ***Cross out all errors with a single line so that the underlying text is still clearly legible.*** Date when the cross-out was made, explain it briefly, and initial or sign it. In some settings, cross-outs must also be witnessed.
10. ***Note all problems; never try to obscure, erase, or ignore a mistake; be honest.*** Be objective; avoid derogatory statements about your ideas.
11. ***Date and sign each page. In many laboratories a corroborating witness should also sign and date the page.*** The scientist and, where relevant, the witness should verify that there are no blank spaces on the pages, that all tables are complete, and that the page is complete. If corrections are later made to an entry, the corrections should be signed and dated by both the scientist and witness.
12. ***Be certain that the laboratory notebook is stored in a secure location.***

Table 6.4. TYPICAL COMPONENTS OF A LABORATORY NOTEBOOK

1. ***In the front of the notebook: the person to whom the book is assigned, the project, the date of assignment, the company/institution, and any other identifying information.***
2. ***A table of contents on the first pages.*** The table of contents should include page numbers and descriptions with sufficient detail to allow easy searching of the notebook's contents.
3. ***For each project, a listing of the results of any literature search and any experimental information collected from colleagues.***
4. ***A page number on every page in consecutive order.***
5. ***Dates, titles, and descriptions.*** Begin the record of each day's work with the date, title, and description of the objectives for the work. It is common to begin each day on a new page with a diagonal line drawn across the unused part of the previous day's page.
6. ***The rationale for each activity performed.*** Documenting ideas is important.
7. ***Any relevant equations or calculations.***
8. ***Complete descriptions of all instrumentation (including models and serial numbers), chemicals used (including manufacturers, catalog and lot numbers, and expiration dates), reagents used (including recipes or references to SOPs), supplies used, samples assayed, standards or reference materials used.***
9. ***Procedural details.*** If an SOP or protocol from the researcher's institution or company is followed, it should be referenced in a unique fashion (e.g., by title and revision date, and/or by ID number). It is usually not necessary to copy an SOP or protocol into the notebook, but any deviations and their justification should be noted. If a procedure comes from a compendium, journal, book, or manual, the complete reference for the procedure should be cited and it may be necessary to record procedural details in the laboratory notebook.
10. ***Sample information.*** When samples are tested, information should be provided regarding their source, storage, identifying information, disposal, and so on.
11. ***Data.*** Data take many forms, for example, values read from instruments, color changes observed, photos, and instrument printouts. Printouts from instruments, photos, and other paper data are generally signed, dated, and securely taped into the laboratory notebook with a permanent adhesive. It is common to sign or write across both the inserted paper and the page on which it is taped in order to authenticate the paper's placement on the page. There should be an explanation of the data provided with it. If data cannot be affixed in the notebook, they may be titled, signed, explained, dated, and filed securely. The data and storage location should be referenced in the laboratory notebook.
12. ***Observations.*** Observations might include, for example, changes in pH or temperature, humidity readings, and instrument operational parameters.
13. ***A brief summary of the work completed.***
14. ***A conclusion and brief interpretation of data collected is usually appropriate.*** For example, if a particular line of investigation is pursued on the basis of preliminary results, note this in the laboratory notebook. Such decisions may be relevant in patent disputes at a later date.

happened in the laboratory. It is common to outline in a laboratory notebook what one *intends* to do; these plans should be written in the present or future tense. What *actually* occurred must be clearly recorded using the past tense.

Another challenge is that a laboratory notebook must be chronological—it must keep moving forward in time. A researcher might be working on more than one project, in which case it is often simplest to keep a different laboratory notebook for each project. If only one laboratory notebook is used, it is not correct to leave empty pages or spaces on a page in order to fill them in later. Rather, if a researcher returns to a project after recording information on something else, it is correct to state at the top of the page that the work is "continued from page___".

Laboratory notebooks should be witnessed whenever research might lead to a patent. The witness, who is not one of the inventors, reads, signs, and dates each entry. The witness should be sure that he/she understands the entries because the witness is corroborating that the work described really happened. It is preferable that the witness is someone who actually observed the experiments, though this may not be possible in practice. In a company that is regulated, laboratory notebooks are also witnessed. The witness must carefully look for mistakes or omissions, such as an erroneous calculation or a missing date. These mistakes are then corrected, briefly explained, signed by both the researcher and witness, and dated. After a notebook is witnessed, no changes should be made to that page. Ideally notebooks should be witnessed every day.

Figure 6.1 shows an annotated laboratory notebook that illustrates some of these ideas.

C. Other Documents That Are Common in Laboratories

i. STANDARD OPERATING PROCEDURES

Most production facilities and many laboratories use procedures to instruct personnel in how to perform particular tasks. A **procedure** *is a written document that provides a step-by-step outline of how a task is to*

434

Continued from page 3 (1)

PROJECT: TAT3 Blockers

Page 4

Date: Jan 3 '08

Title: Inhibition of MabTAT3 binding by test compounds ANTAT3-1 and ANTAT3-10 (2)

Purpose: To test compounds ANTAT3-1 and ANTAT3-10 (3) for their ability to competitively block antibody binding to TAT3. As described (nbk. 425, p.1). We have isolated a cell surface molecule, TAT3, involved in spermatozoa maturation and development. Monoclonal antibody MabTAT3 binds TAT3 with high affinity. Testing and preparation is described in nbk. 426, pp. 67-92. TAT3 is characterized in nbk. 425, pp. 5-32. The preparation and initial screening of ANTAT3-1 and ANTAT3-10 is described in nbk. 432, pp. 1-22. (5)

Methods: (6) ATCC cell line 7456A was cultured and plated (10⁴ cells/well) (4) in 35 mm² wells and grown to confluency. Culturing conditions are described in nbk. 425, p. 3. ANTAT3-1 and ANTAT3-10 were diluted in HBSS (GIBCO) in 10-fold dilutions ranging from 4×10^{-3} ug/ml to 40 ug/ml. MabTAT3 was diluted from a stock solution of 25 ug/ml and used at between 0.05 ug/ml and ~~10 ug/ml 15 ug/ml~~ obtained from MLP. (15)

(8) 10 ug/ml MabTAT3 (7)

JCL 1/4/08 Ran out of reagent (9)

(10) Samples were distributed in the cell samples as diagrammed on page 5. Cells were incubated for 2 hrs, 37 C and harvested and lysed as described (nbk. 426, p. 140). MabTAT3 bound to 7456A cells was quantitated by modified ELISA described in nbk. 432, p. 80. Raw data are provided on p. 6. (11)

(12) Results: The experiment failed, no ANTAT3-1 or ANTAT3-10 binding was detected in any of the wells except at the highest doses, but I think this is an artifact. (13)

(14) 1/3/08 Title: Abiloty of ANTAT3-1 and ANTAT3-10 (16) to inhibit spermatozoa maturation in mice.
Method: BalbC mice were injected i.p. with 0.5 ml of a 1 mg/ul solution of

Work continued to page 5

Signature: Julie Lawson	Date: January 3, 2008 (17)
Read and Understood by: (18)	Date: March 10, 2008 (19)
Read and Undersood by:	

(a)

Figure 6.1. An Annotated Laboratory Notebook. a. Notebook page. **b.** Legend.
Source: Based on a laboratory manual page and reprinted with permission from Merchant and Gould Legal Firm.

be performed. Such documents are often called **standard operating procedures (SOPs),** although other names are used as well. For example, a research laboratory might simply call these "procedures" (or even "protocols," although this term has another meaning as explained in Table 6.2). Everyone follows the same procedures to assure that tasks are performed consistently and correctly. Standard operating procedures