THE BUDAPEST TREATY:

CODE OF PRACTICE FOR IDAs

EDITOR: M. BOSSCHAERTS, BCCM™

October 1998

THE BUDAPEST TREATY: CODE OF PRACTICE FOR IDAs

TABLE OF CONTENTS

0. INTRODUCTION 3

1. OBLIGATIONS OF THE DEPOSITOR 5

- ACCORDING TO THE BUDAPEST TREATY 5
- PRACTICALITIES 6

  - Information concerning the cultivation, storage and viability testing of the mo 6
  - Mixed cultures 6
  - Unofficial notifications to the depositor 7
  - Payment for a deposit 7
  - Withdrawal of a deposit 7
  - Conversion of deposits originally made outside the purview of the BT 11
  - Co-deposit by more than one depositor 11
  - Selling of the rights on a deposit 11
  - Depositor versus applicant of a patent 12

2. OBLIGATIONS OF THE IDA 13

- ACCORDING TO THE BUDAPEST TREATY 13
- PRACTICALITIES 16

  - Test methods and criteria for viability testing 16
    - for fungi and yeasts
    - for bacteria
    - for plasmid bearing (genetically modified) mo
    - for isolated plasmid DNA
    - for bacteriophages
    - for plant cell cultures
    - for plant viruses
    - for plant seeds
    - for animal cell cultures
    - for animal viruses
  - Contamination of deposited cultures 20
  - Responsibility for authenticity and purity of the deposited cultures 20
  - Requests for information about a deposited culture or the related deposit documents 21
  - End of the period of storage 22

ANNEXES

O. INTRODUCTION

Patent law requires the public disclosure of all relevant details pertaining to an invention. Written descriptions and drawings are normally adequate and sufficient for the purpose of seeking patent protection, but this is not the case when the invention involves e.g. microorganisms. To rectify such cases, the deposit of the biological material within an officially recognized culture collection was deemed necessary for the patenting procedure.

This principle was endorsed in the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. Concluded on April 28, 1977, and enacted on August 19, 1980, the Budapest Treaty (BT) acknowledges that, for all signatory States, a deposit made with one of the "International Depositary Authorities, IDAs" (i.e. a culture collection recognized as such by the World Intellectual Property Organization, WIPO) is sufficient for the purpose of their respective patent procedure(s).

While the Budapest Treaty (BT) and its Regulations constitute a sound basis for delimiting the duties and responsibilities of culture collections with IDA status, it was stated from the beginning by representatives of the World Federation for Culture Collections (WFCC) that the BT did not always formulate explicit solutions for all circumstances. This issue was newly raised at the annual meeting of the European Culture Collections' Organization (ECCO) in Slovenia (July 3-4, 1995). Participants felt that the BT is open to interpretation and each IDA maintains its own procedures. In order to harmonize the way IDAs resolve certain issues, it was decided to compile an inventory of the procedures applied by IDAs.

The Belgian Coordinated Collections of Microorganisms, BCCM™ was mandated to coordinate this initiative. Responses to a questionnaire sent in July 1995 to all ECCO members with IDA status were reviewed and summarized in January 1996.

A workshop was held in February 1996 in Brussels to discuss the replies *(Annex 1: List of participants)*. Separate working groups were established to collect additional pertinent information about the day to day operations of IDAs *(Annex 2: Working group coordinators)*.

A second workshop held in Veldhoven, August 1996 during the meeting of the World Federation for Culture Collections (WFCC) was used as an opportunity to solicit the representatives from non-European IDAs for their comments and suggestions (*Annex 3: List of participants*).

Experts with the World Intellectual Property Organization (WIPO, Geneva) and the European Patent Office (EPO, Munich) were informed about this initiative and contributed other valuable information.

The resulting Code of Practice for IDAs aims to ensure, as far as opportune, that all IDAs apply similar principles and procedures for the handling of deposits. Ultimately, this coordination is advantageous for depositors, and it confirms the intent of the BT to harmonize the requirements for patent deposits.

The Code of Practice summarizes the points on which a minimal consensus exists among IDAs and provides practical guidelines for dealing with unclear cases or situations in the patent deposit procedure.
It should be remarked that this Code of Practice is not final. It can always be updated, clarified or extended if necessary.

The purpose of this Code of Practice is not to deny the particular identity or policy of any IDA.

Each IDA may impose additional requirements in order to comply with internal or national regulations.

Note: Abbreviations

IDA	International Depositary Authority
BT	Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and Regulations
mo	microorganism(s) or biological material

NB The term “microorganism” is not defined in the BT. It may be interpreted in a broad sense. Whether an entity is technically a microorganism matters less in practice than whether the deposit of that entity is necessary for the purposes of disclosure. For example, tissue cultures and plasmids can be deposited under the terms of the BT though they are not microorganisms in the strict sense of the word.

EPO	European Patent Office
WIPO	World Intellectual Property Organization
ECCO	European Culture Collections’ Organisation
WFCC	World Federation for Culture Collections

1. OBLIGATIONS OF THE DEPOSITOR

➢ ACCORDING TO THE BUDAPEST TREATY

To make an original deposit the depositor should:

1.1. **Transmit the microorganism** (mo) to the IDA *(rule 6.1.)*

NB The shipping of mo is subject to national and international regulations.

1.2. **Transmit** to the IDA **a written statement** *(rule 6.1.)* containing:

- the signature of the depositor
- an indication that the deposit is made under the BT
- an undertaking not to withdraw the deposit for the period specified in *rule 9.1*.[(a)]
- the name and address of the depositor
- detailed instructions for the cultivation and storage of the mo, and for the testing of its viability [(b)]
- an identification reference (number, symbols, etc.) given by the depositor for the mo
- an indication of the properties of the mo which are or may be dangerous to health or the environment, or a declaration that the depositor is not aware of any such properties
- [(c)]

(a) *Rule 9.1.* specifies that the deposited mo is to be stored for a period of at least 5 years after the most recent request for the furnishing of a sample of the deposited organism was received by the IDA and, in any case, for a period of at least 30 years after the date of the deposit.

(b) Where a mixture of mo is deposited, the written statement must also contain descriptions of the components of the mixture and at least one method that would allow for the verification of their presence.

(c) It is strongly recommended that the written statement should contain the scientific description and/or proposed taxonomic designation of the deposited mo.

1.3. **Fulfil all additional requirements** of the IDA [(d)] *(rule 6.3.)*:

- deposit the mo in the form and quantity necessary for the purposes of the BT and its Regulations
- furnish a duly completed form established by the IDA for the purposes of the administrative procedures of the IDA
- draft the written statement (cf. 1.2.) in the language specified by the IDA
- pay the storage fee
- to the extent permitted by the applicable law, enter into a contract with the IDA defining the liabilities of the depositor and the IDA

(d) The IDA is to forward any such requirements and/or other amendments thereof to the International Bureau (see article 2 (xiii) of the BT).

➢ PRACTICALITIES

Information concerning the cultivation, storage and viability testing of the mo

In most cases the depositor provides the relevant information concerning the cultivation, storage and viability testing of the mo. Most IDAs request this information on an 'Accession form'.

If this information is missing, the requirements of *rule 6.1.* are not fulfilled. Until this information has been presented and viability has been demonstrated, the IDA can not accept the mo, and consequently, the IDA is not to forward the international form BP/4 (Receipt and Acceptance) or BP/9 (Viability statement). Depositors should be aware that insufficient information can delay the completion of the viability test.

The IDA shall notify the depositor immediately that information is missing and invite him to comply with the specified requirements (*rule 6.4.(b)*). In practice this is done either by phone, fax, e-mail or in writing *(cf. model form I)*.

Given the IDA's scientific expertise, this lack of information is often not a technical difficulty but merely an administrative problem. As such, the IDA may continue the deposit procedure applying its own standard methods for preservation and cultivation. If necessary the IDA should discuss with the depositor whether these methods are appropriate.

The date of receipt of the viable biological material becomes the date of deposit, but only once the depositor has complied with all his obligations.

Mixed cultures

Most IDAs accept mixed cultures.

The deposit of a mixed culture is however not without difficulties. Due to antagonism and different growth rates, for example, testing the viability of the different components of the mixture can be problematic. Also, it is not obvious that the composition of the mixture will remain the same after preservation.

For these reasons, most IDAs recommend that the depositor separates the different components and deposits them individually.
In such cases, the depositor is charged for each separate deposit.

If, however, a component can not be readily dissociated (e.g. organisms living in symbiosis) the mixture might be deposited. The depositor is obliged to provide the IDA with a description of the components of the mixture and at least one method that would allow for the verification of their presence. The IDA will accept the mixture on the conditions that it is possible to test the viability of each of the organisms in the mixture individually and it is possible to ensure that the mixture can be preserved without losing one of the components.

Unofficial notifications to the depositor

In principle, the IDA does not inform the depositor about the deposit date and the "provisional" accession number until the viability of the mo has been demonstrated. Nevertheless in exceptional cases (to be decided by the IDA on an *ad hoc* basis) the IDA can give this information "unofficially" to the depositor. This can be done by phone, by e-mail or by fax. The depositor must acknowledge that this information becomes official only on completion of the viability test and on issue of the forms BP/4 and BP/9. Also, he must realize that any use of unofficial information is at his own risk.
To avoid abuse of this information an appropriately worded document should be used. For this purpose *model form II* can be used.

NB In case of a European patent application the depositor does definitely not need the information about the deposit date and accession number at the date of filing his patent application. This information can be forwarded to the depositor at a later time.

NB Some IDAs only assign the accession number once viability and purity of the culture have been proven. These IDAs can obviously not communicate “provisional” accession numbers to the depositor (cf model form III).

Payment for a deposit

The IDA has accepted the deposit once the international forms BP/4 and BP/9 have been forwarded to the depositor. At such time, the deposit is to be regarded as valid according to the Budapest Treaty.
The payment for a deposit is a matter of contractual agreement between the IDA and the depositor. Therefore, the IDA may decide not to issue form BP/4 (Receipt and Acceptance) until arrangements for payment have been made.

Withdrawal of a deposit

The depositor can not withdraw the deposit for the period specified in *rule 9.1*[(a)]. An IDA may accept the withdrawal of a deposit only on the condition that the international forms BP/4 (Receipt and Acceptance) and BP/9 (Viability statement) have not yet been sent to the depositor.

However, the deposit procedure is to be regarded as complete from the date these forms have been forwarded, and the depositor may not withdraw the deposit.

(a) *Rule 9.1.* specifies that the deposited mo is to be stored for a period of at least 5 years after the most recent request for the furnishing of a sample of the deposited organism was received by the IDA and, in any case, for a period of at least 30 years after the date of the deposit.

MODEL FORM I: Additional information requirement

(*Depositor's name and address*)

Date

Dear ...,

I am pleased to acknowledge the receipt of (*number*) cultures that you wish to deposit with the (*name of the IDA*) under the Budapest Treaty.

Your cultures arrived on (*date*) in good condition.

The (*name of the IDA*) kindly invites you to provide some additional information concerning the appropriate *preservation method/cultivation method/viability test* for the deposited cultures.

According to Rule 6.1. (a) iii of the Budapest Treaty the (*name of the IDA*) can not officially accept the cultures until this information has been given.

Please do not hesitate to contact me if you have any questions.

Yours sincerely,

....

The words in italics are to be adapted for each case.

MODEL FORM II: Unofficial notification of deposit date and accession numbers

(*Depositor's name and address*)

Date

Dear ...,

I am pleased to acknowledge the receipt of (*number*) cultures that you wish to deposit with the (*name of the IDA*) under the Budapest Treaty.

Your cultures arrived on (*date*) in good condition and have been assigned the following unofficial accession numbers:

(*accession number*) was assigned to (*identification reference*)
(*accession number*) was assigned to (*identification reference*)

Viability test procedures have been started.

As soon as the viability of the cultures has been confirmed, the (*name of the IDA*) will forward to you the international forms BP/4 ('Receipt of an original deposit') and BP/9 ('Viability statement'). Please be advised that the deposit date and accession numbers will become official only on receipt of these forms. Until such time, the (*name of the IDA*) does not accept any responsibility for the use of any information contained herein.

Yours sincerely,

....

The words in italics are to be adapted for each case.

MODEL FORM III: Unofficial notification of the deposit date

(*Depositor's name and address*)

Date

Dear ...,

I am pleased to acknowledge the receipt of (*number*) cultures that you wish to deposit with the (*name of the IDA*) under the Budapest Treaty.

Your cultures arrived on (*date*) in good condition.

Viability test procedures have been started.

As soon as the viability of the cultures has been confirmed, the (*name of the IDA*) will forward to you the accession numbers assigned to them as well as the international forms BP/4 ('Receipt of an original deposit') and BP/9 ('Viability statement').
Please be advised that the deposit date will become official only on receipt of these forms. Until such time, the (*name of the IDA*) does not accept any responsibility for the use of any information contained herein.

Yours sincerely,

....

The words in italics are to be adapted for each case.

Conversion of deposits originally made outside the purview of the BT

The BT contains no restrictions as to the source of the deposited material. After having made a deposit outside the BT (e.g. safe or public deposits, or deposits formerly made under national patent law) with an IDA, a depositor may subsequently convert such a deposit to a deposit under the BT without it being necessary for him to redeposit the mo, provided that he complies with all requirements of the BT.

The date of deposit remains the date on which the IDA received the viable organism. It is essential to remember that the date of request for conversion comes prior to the filing date of the patent application. As such, it is imperative in all cases of conversion that both the date of deposit and the date of receipt of the request for conversion must be stated on the international form BP/4 (Receipt and Acceptance). The legal status and consequences governing the deposit during the period between these two dates is determined by national law.

If an IDA receives a culture for other purposes than to make a deposit (e.g. for an identification), and subsequently the depositor wishes to deposit this culture for patent purposes, the date of receipt of the culture for the first purpose is not to be accepted as date of receipt of the patent deposit. If sufficient material is still available at the IDA, the depositor does not need to transmit additional material. Since this kind of deposit is not to be regarded as a conversion but as an original deposit, the date of receipt of the request is to be designated as the deposit date.

Of course in all these cases *rule 6.4.d* retains priority; it states that the earliest date on which an IDA can accept a deposit under the Budapest Treaty is the day it acquired the status of International Depositary Authority.

NB To ensure the authenticity of the involved biological material the IDA should send a sample of the material to the depositor and request him to verify the identity of the culture (see also 'Responsibility for authenticity and purity of the deposited cultures').

Co-deposit by more than one depositor

It is possible that two or more depositors may wish to deposit a culture under the BT together. For practical reasons one of the depositors should be identified as the primary contact person when communicating with the IDA.

Selling of the rights on a deposit

An IDA deals directly and exclusively with the original depositor. However, if the rights on a deposit are sold, or if the name of the depositor is changed, the original depositor (or his successor in title) should notify the IDA. At such time, the IDA can contact both relevant parties to request written confirmation of any such changes. The IDA will then communicate with the party that proved to have the actual rights on the deposit.

Depositor versus applicant of a patent

The depositor is not necessarily the same person as the applicant of the patent referring to the deposited material. In this case, the depositor should authorise the applicant to make clear reference to the biological material in the patent application and should also give his fully informed and irrevocable consent that the deposited material is to be made available to the public.
Such authorisation does not affect the relationship between the depositor and the applicant or change the position of the authorised applicant. The latter remains a third person within the terms and intended scope of the BT and may obtain a sample under the conditions prescribed in rule 11.2 (ii) (i.e. with the depositor's agreement) or rule 11.3 (iii) (i.e. applicant as a legally entitled party).

However, if it is apparent from a certified request for release of samples pursuant to rule 11.3. that the depositor and the applicant are not identical and the IDA has doubts whether the applicant has been authorised, the IDA should not release the sample but notify the relevant patent office immediately. In the absence of such an authorisation by the depositor, the certification by the patent office is deemed invalid and, consequently, the conditions of rule 11.3 (iii) are not fulfilled.

The depositor should provide the IDA with a letter stating the name of the applicant who is authorised to refer to the deposit in a patent application.

2. OBLIGATIONS OF THE IDA:

➢ **ACCORDING TO THE BUDAPEST TREATY**:

In respect of each culture of a mo deposited with it (or transferred to it) the International Depositary Authority shall:

2.1. **accept the mo** when all requirements referred to in 1.1., 1.2. and 1.3. are complied with [(e)] (*rule 6.4*.).
The IDA shall refuse to accept the mo where [(f)]:
- the mo is not of a kind of mo to which assurances furnished under *rule 3.1.(b)(iii)* or *3.3.* extend
- the properties of the mo are so exceptional that the IDA is technically not in a position to perform the tasks prescribed by the BT and the Regulations
- when the deposited mo is received in a condition which clearly indicates that the mo is missing or which for scientific reasons precludes acceptance of the mo

(e) If any of these requirements is not complied with, the IDA shall immediately notify the depositor of this fact and invite him to comply with the specified requirements.

(f) In case the IDA refuses to accept the deposited mo, the IDA shall immediately notify the depositor in writing thereof, indicating the reasons for the refusal.

2.2. **issue** to the depositor **a receipt** in attestation of the fact that it has received and accepted the mo *(rules 7.1., 7.2., 7.3.)*. This receipt shall be established on an 'international form BP/4' and shall bear the signature of the person(s) having the power to represent the IDA or that of any other official of that IDA duly authorized by the said person(s) [(g)].
This receipt shall indicate that it is issued by the depositary institution in its capacity of IDA under the BT and shall contain:
- the name and address of the IDA
- the name and address of the depositor
- the date of the original deposit [(h)]
- the identification reference (number, symbols, etc.) given by the depositor to the mo
- the accession number given by the IDA to the deposit
- where the written statement (cf. 1.2.) contains the scientific description and/or proposed taxonomic designation of the mo [(c)], a reference to that fact

(g) Any words or letters in the receipt or in the viability statement in characters other than those of the Latin alphabet shall also appear therein transliterated in characters of the Latin alphabet.

(h) When the mo has been accepted as an original or new deposit, the date of that original or new deposit, as the case may be, shall be the date on which the mo was received by the IDA (*rule 6.4.c.)*

(c) It is strongly recommended that the written statement contains a scientific description and/or proposed taxonomic designation of the deposited mo.

2.3. **store the deposited mo** with the sufficient and due care necessary to keep it viable and uncontaminated, for the period specified in *rule 9.1*[(a)].

[(a)] *Rule 9.1.* specifies that the deposited mo must be stored for a period of at least 5 years after the most recent request for the furnishing of a sample of the deposited organism was received by the IDA and, in any case, for a period of at least 30 years after the date of the deposit.

2.4. **deny access to information to anyone** whether a mo has been deposited with it under the BT. Furthermore, it shall not give any information to anyone concerning any mo deposited with it under the BT [(i)] *(rule 9.2.)*

[(i)] except to an authority, natural person or legal entity which is entitled to obtain a sample of the mo under *rule 11* and subject to the same conditions as provided in that rule.

2.5. **test the viability** of each mo deposited with it *(rule 10.1.)*:
- promptly after any deposit or any transfer
- at reasonable intervals, depending on the kind of mo and its possible storage conditions, or at any time, if necessary for technical reasons
- at any time, on the request of the depositor

2.6. **issue a statement concerning the viability** of the deposited mo *(rule 10.2.)*. This viability statement [(j)] shall indicate whether the mo is or is no longer viable and shall contain:
- the name and address of the IDA
- the name and address of the depositor
- the date of the original deposit or, where a new deposit or a transfer has been made, the most recent of the dates of the new deposit or the transfer
- the accession number given by the IDA
- the date of the test to which it refers
- the information on the conditions under which the viability test has been performed, if the results of the tests were negative and if requested by the party to which the viability statement is issued

This viability statement shall be established on an 'international form BP/9' and shall bear the signature of the person(s) authorized to represent the IDA or that of any other official of that IDA duly authorized by the said person(s) [(g)].

[(j)] A viability statement shall be issued to:
- the depositor, promptly after any deposit or any transfer
- the depositor, on his request, at any time after the deposit or transfer
- any industrial property office, other authority, natural person or legal entity, other than the depositor, to whom or to which samples of the deposited mo were furnished in conformity with *rule 11*, on his or its request, together with or at any time after such furnishing of samples

[(g)] Any words or letters in the receipt or in the viability statement in characters other than those of the Latin alphabet shall also appear therein transliterated in characters of the Latin alphabet.

2.7. **furnish samples** of the deposited mo
- to interested industrial property offices *(rule 11.1.)*
- to the depositor or to third parties with the written authorization of the depositor ('authorized parties') *(rule 11.2.)*
- to parties legally entitled ('certified parties' or 'requesting parties') *(rule 11.3.)*

2.8. **notify the depositor** of *(rule 11.4.)*:
- the fact that a sample is furnished to any interested party other than the depositor

- the date on which this sample was furnished
- the name and address of the industrial property office, the authorized party, the certified party or the requesting party, to whom or to which the sample was furnished

This notification shall be accompanied by a copy of the pertinent request, of any declarations submitted under *rules 11.1.* or *11.2.(ii)* in connection with the said request, and of any forms or requests bearing the signature of the requesting party in accordance with *rule 11.3.*.

➢ PRACTICALITIES

Test methods and criteria for viability testing

The IDA is obliged to test the viability of each deposited mo. Hence the depositor must provide the information necessary to perform the test.

In general the testing of the purity of the deposited cultures is performed simultaneously with the viability test.

Although the identity of the mo is not checked extensively, procedures for purity control commonly bring, to a varying degree, attention to the taxonomic positioning of the mo. If the IDA notices discrepancies between the identity or the properties of the organism and the description given by the depositor, it is recommended that the IDA notifies the depositor of this fact. The depositor can then check the authenticity of the deposited culture.
If during the course of discussions about the identity of the organism the IDA is required to take further action (e.g. carry out the identification of the mo), the depositor may be charged for this additional service.

NB It should be remarked that, according to the Budapest Treaty, the depositor is recommended but not obliged to give the scientific description of the organism or he may give this information later. National laws or restrictions concerning the kinds of mo accepted by the IDA, however, might oblige the depositor to indicate the taxonomic designation of the strain.

Test procedures and criteria for viability vary according to the type of mo. The following principles and minimal criteria are applied to the type of cultures listed below.

For fungi and yeasts:

To test the viability of fungi and yeasts IDAs inoculate the organism onto the recommended media and incubate under the recommended conditions. Viability is proven by observation of growth of the organism (i.e. visible increase of cell material).

Purity is verified macroscopically and microscopically.

For bacteria:

To test the viability of bacteria IDAs inoculate the organism onto/into the recommended media and incubate under the recommended conditions.
Colony formation or increase in cell number (in case of liquid cultures) must be observed.

Starting from an active culture, the minimal criteria for confirming viability range from 10 - 12 colonies from the original biomass to 1 colony provided that this single colony can be successfully subcultured. The colonies obtained should look "normal" and should be of the type expected for the particular bacterium being deposited.

In cases where only a few colonies are obtained from frozen or freeze-dried preparations and where the IDA does not propagate the material, one of the following options can be taken:

1. request replacement samples from the depositor, repeat the viability test and issue

BP/9 if the new samples are cultured successfully. In this case, the date of receipt of the replacement samples is deemed the date of deposit.

2. issue a viability statement (BP/9) but immediately request new samples under *rule 6.2.* of the BT.

Since option 2 can not guarantee the viability of the replacement samples, option 1 is to be preferred.

Examination of purity is usually done macroscopically (colony morphology) and microscopically (cellular morphology). If both cell and colony morphology appear to be the type expected for the bacterium being deposited, then these observations are considered to be sufficient for issuing BP/4 and BP/9.

For plasmid bearing (genetically modified) mo:

To test the viability of plasmid bearing (genetically modified) mo, the organism is inoculated on an appropriate selective medium. Viability is proven by growth of the organism on this selective medium.

To check the purity, the organism is streaked on the appropriate medium with and without selective pressure. In addition, microscopic analysis is recommended.

NB The taxonomic designation and the indicated plasmid size should be verified in case of doubts about the designation indicated by the depositor or if these examinations must be conducted due to other regulations.

For isolated plasmid DNA:

The presence of plasmid DNA is proven electrophoretically in an agarose gel. At the same time the approximate amount and the size of the DNA can be estimated.
The viability of the plasmid is proven by the transformation of a suitable host with the plasmid and the subsequent inoculation of this host/plasmid combination onto a selective medium.

NB
- In special cases the restriction pattern of the plasmid DNA can also be determined.
- Other examinations might be necessary in order to comply with other regulations.
- In case it is not available in the public collection the depositor should also supply a suitable host strain.

For bacteriophages:

The viability of phages is tested by applying the spot-test or by plating bacteria and phages together in a top layer.

The number of plaque-forming units (pfu) per ml of lysate is determined by the serial dilution method or by the spot titre method. A minimum of 10^7 pfu/ml is required to have a sufficiently safe quantity to store the lysate for the purposes of the BT.

Purity of the phage lysate can be tested by streaking the lysate on an uninoculated agar plate.

NB The depositor should also supply a suitable host strain, if it is not available in the public collection.

For plant cell cultures:

When plant cell cultures are deposited in the form of a callus, viability is proven by growth on an appropriate medium. A definite increase of cell mass must be observed.
For samples in the form of a suspension culture, growth in an appropriate medium must result in a definite increase in cell density. Frozen samples are first thawed and transferred to an appropriate medium. The growth of the cells is observed until the cell mass has at least doubled.

The viability test will be deemed negative, if the cell number has not increased considerably (i.e. doubled) after a period of at least two months.

Depositors should be encouraged to give the normal growth characteristics of the culture. This information will assist the IDA make the appropriate determination as to viability.

The purity of the cell culture is checked by microscopic examination. If contamination with microorganisms is suspected, further tests are to be conducted.

NB
- To test the viability of plant cells several laboratory tests are available (FDA, TTC, reduction). Nevertheless, because a positive result obtained from one of these tests does not guarantee that a cell culture will regrow after cryopreservation, the result of the viability test must be based on the observation of obviously growing cultures.
- Since plant cell cultures may be mixed populations of genetically different cells (ploidy changes, chromosome changes and transposon activation occur in cell cultures), tests must be conducted to determine whether cryopreservation changes the specific characteristics of a cell culture.

For plant viruses:

In order to revitalize the virus in desiccated infected leaves the leaves are to be ground with a few drops of inoculation buffer until a green paste is achieved. This paste is to be diluted with inoculation buffer to yield 2-3 ml of final inoculum. The inoculum is to be rubbed onto the leaves of the appropriate propagation host(s) which had been dusted with a sterile abrasive, such as Celite or Carborundum. After a few minutes the inoculated leaves are to be rinsed with tap water.

For plant seeds:

Germination is the sole criterion for the determination of seed viability.
Germination can be considered to occur at the initial imbibition stage or at the emergence and development of a seedling. For the purposes of a patent deposit, however, the first sign of radical emergence constitutes germination and hence viability.

For plant seeds, viability should not be confused with storage ability or longevity of the

deposit. Although in principle a single seed germinating in a batch of 400 can render the batch viable, it is preferred that 85% of the seeds germinate.
If less than 85% of the seeds germinate, the depositor must be notified that it is unlikely that his deposit will survive the 30 years storage period and that a new deposit will be required at a later stage. This eventuality can be covered under *rule 6.2.*.

NB - If required by the guidelines specified by the International Board for Plant Genetic Resources (IBPGR) or the International Seed Testing Association (ISTA), all seeds tested should be germinated under dormancy breaking procedures.
- Alternative methods for viability testing, e.g. tetrazolium topography, should be used only in exceptional circumstances and then only by suitably trained personnel.

For animal cell cultures:

For animal cell cultures a minimum number of 4 x10^6 viable cells per ampoule (or 2 x 10^6 cells for adherent cultures) is required to confirm viability. For an acceptable deposit a good recovery and growth of the cells must be observed. Growth can be measured by counting the cells in a counting chamber. The number of viable cells must increase within one and a half weeks.

The purity of the culture is to be rigorously verified against the presence of bacteria (mycoplasma, etc.) and fungi.

For animal viruses:

Viability tests are performed *in vivo* on eggs and on primary cells.
Many different assays can be used to test the viability of animal viruses, e.g. RT assays.
A minimum number of infective particles corresponding at least to 100 times the minimum detectible level is required.

Viruses are checked for purity against the presence of bacteria (mycoplasma, methylotrophic bacteria, etc.) and fungi.

NB If the most appropriate host cell is not generally available to the public, it must be supplied by the depositor.

Contamination of deposited cultures

Each IDA must refuse the deposit of contaminated cultures.

If the culture transmitted by the depositor is impure, two solutions are possible:

1. The IDA notifies the depositor of its inability to accept the culture (the acceptance of the mo is precluded for scientific reasons) and requests that he transmits another, pure culture. In this case the date of deposit changes.

2. The IDA may offer to the depositor the possibility to purify the culture. In this case the date of deposit remains the date of receipt of the material since the IDA has already disposed of the organism. To be absolutely sure that the correct culture is deposited, however, the IDA must send a sample of the purified and preserved culture to the depositor with the request to verify the authenticity of the culture. The depositor is to be advised that if he does not confirm or reject the authenticity of the culture in a written statement within a certain time limit (e.g. three months), the culture will be considered to be the correct one (see also 'Responsibility for authenticity and purity of the deposited cultures').
If the depositor notices that the wrong organism has been isolated, he must make a new deposit and, consequently the deposit date changes.
The depositor is to be aware that he may be charged for the purification service that the IDA conducts.

The first solution is to be preferred. Therefore depositors should be encouraged to start the deposit procedure in time, thereby avoiding the more cumbersome second option.

Responsibility for authenticity and purity of the deposited cultures

In practice the IDA and the depositor share the responsibility for the purity of the deposited culture.
The depositor must ensure that a pure culture is transmitted to the IDA (if more than one component must be present, the culture is to be recognized as a 'mixed' culture).

The IDA must check the purity of the culture before accepting it and must notify the depositor if any contaminants are found. Also, the IDA must take all the necessary measures to ensure that the culture remains uncontaminated.

The final responsibility for the authenticity of the culture lies with the depositor. The IDA is not obliged to check the identity or the performance (e.g. product expression) of the culture. Most IDAs are technically not in a position to perform this task. Nevertheless, it is important that the IDA takes such measures as are needed to enable the depositor to fulfil his responsibilities.

If it is the case that the IDA must propagate the material in order to have sufficient material to preserve the mo, the IDA must send a sample of the propagated material to the depositor and request him to verify the authenticity of the culture. As before, the depositor should be made aware that if he does not provide a written confirmation or rejection of the authenticity within a certain time limit (e.g. three months), the propagated material is to be regarded as identical to the original deposited culture *(see also 'Contamination of deposited cultures')*. In case the authenticity of the culture has been rejected, the IDA must ask the depositor to transmit a new sample of the culture. According to rule 6.2 the depositor has to add, among other things, a written statement alleging that the mo which is the subject of the new deposit

is the same as that which was the subject of the previous deposit.

When a sample of a culture for which the IDA did not receive a confirmation or rejection of authenticity is to be furnished to a third party, the IDA should provide a statement that "the culture has not been checked by the depositor".

Request for information about a deposited culture or the related deposit documents

According to rule 9.2. the IDA should not disclose information that a particular mo has been deposited with it under the BT.

Information about a deposit is given only to the person who, after request, is entitled to obtain a sample of the deposited mo according to rule 11 of the BT.
According to rules 11.4. and 7.6., this person is also entitled to receive the following information:

- the accession number given to the deposit
- a copy of the receipt (international form BP/4)
- an indication of any properties of the mo which are or may be dangerous to health or to the environment
- upon request, an indication of the conditions which the IDA employs for the cultivation and storage of the mo
- upon request, the most recent scientific description and/or proposed taxonomic designation of the deposited mo.

This information is to enable the recipient to handle and analyse the microorganism correctly.

Further information (e.g. concerning the relations between the IDA and the depositor, the delivery of samples or any other kind of file inspection) should not be made available to third parties.

All requests for information from parties other than those mentioned in *rule 11*, should be accompanied by the written permission of the depositor.
The IDA should ensure that the necessary criteria are fulfilled before releasing any information. The IDA should also ensure that any request for information, even from the depositor, is given in a written statement.

End of the period of storage

The IDA must store the deposited mo for a period of at least 30 years after the date of deposit (or for a period of at least 5 year after the most recent request for the furnishing of a sample of the deposited organism was received by the IDA).

It is advisable that IDAs make suitable arrangements about what to do with the deposited material when this period is over. Such arrangements should be specified in a contract between the IDA and the depositor. Possible arrangements are:

- destruction of the material
- return the material to the depositor
- make the material available to the public

In the case of absence of such arrangements, civil law is applicable.

ANNEX 1: LIST OF PARTICIPANTS of the ECCO-WORKSHOP, held in Brussels BCCM™ (OSTC), February 12, 1996, on THE BUDAPEST TREATY: DISCUSSION OF THE RESULTS OF THE QUESTIONNAIRE "Inventory of problems and ad hoc solutions in the framework of the deposit of microorganisms for patent purposes under the Budapest Treaty".

Participants:

Dr. M.C. Agterberg	CBS
Mrs. M. Bosschaerts (reporter)	BCCM™
Mrs. Y. Cerisier	CNCM
Dr. T. Dando	NCIMB
Mr. J. De Brabandere (chairman)	BCCM™
Dr. D. Fritze	DSMZ
Dr. M.D. Garcia	CECT
Dr. B. Holmes	NCTC
Dr. D. Janssens	BCCM™/LMG
Mrs. F. Symoens	BCCM™/IHEM
Prof. Dr. F. Uruburu	CECT
Dr. F. van Asma	CBS
Mrs. M. Vanhoucke	BCCM™/LMBP
Dr. V. Weihs	DSMZ

Excused:

Dr. J. Day	CCAP
Dr. A. Doyle	ECACC
Dr. D. Smith	IMI

ANNEX 2: WORKING GROUP COORDINATORS FOR COLLECTING/HARMONIZING THE PROCEDURES AND CRITERIA FOR VIABILITY TESTING OF MICROORGANISMS

Type of microorganism	Coordinator	IDA
Fungi and yeasts	Dr. F. van Asma	CBS
Bacteria	Dr. T. Dando	NCIMB
Plasmids	Dr. V. Weihs	DSMZ
Bacteriophages	Dr. F. van Asma	CBS
Plant cell cultures	Dr. D. Fritze	DSMZ
Plant viruses	Dr. D. Fritze	DSMZ
Plant seeds	Dr. T. Dando	NCIMB
Animal cell cultures	Mrs. Y. Cerisier	CNCM
Animal viruses	Mrs. Y. Cerisier	CNCM

ANNEX 3: LIST OF PARTICIPANTS of the WORKSHOP, held in Veldhoven, August 29, 1996 on THE BUDAPEST TREATY: OPPORTUNITY FOR A CODE OF PRACTICE FOR IDAs?

Participants:

Dr. M.C. Agterberg	CBS
Dr. V. Arunpairojana	TISTR
Mrs. M. Bosschaerts (chair)	BCCM™
Prof. A.-M. Corbisier	BCCM™/MUCL
Dr. T. Dando	NCIMB
Mr. J. De Brabandere	BCCM™
Dr. A. Doyle	ECACC
Dr. D. Fritze	DSMZ
Dr. I. Gandjar	UI Fac. FSI
Dr. B. Holmes	NCTC
Dr. D. Janssens	BCCM™/LMG
Dr. P. Packer	ECACC
Mrs. B. Parodi	ICLC
Dr. R. Roblin	ATCC
Dr. D. Smith	IMI
Dr. G. Stacey	ECACC
Mrs. F. Symoens	BCCM™/IHEM
Dr. M. Uhl	EPO
Prof. Dr. F. Uruburu	CECT
Dr. F. van Asma	CBS
Mrs. M. Vanhoucke	BCCM™/LMBP
Dr. V. Weihs	DSMZ

<u>ANNEX 4</u>: LIST OF IDAs WHO EMPHATICALLY EXPRESSED THEIR AGREEMENT WITH THE PRINCIPLES DESCRIBED IN THE CODE OF PRACTICE FOR IDAs (Situation on 1 November 1999)

ABC	Advanced Biotechnology Center Italy
ATCC	American Type Culture Collection United States of America
BCCM™	Belgian Coordinated Collections of Micro-organisms Belgium
CBS	Centraalbureau voor Schimmelcultures The Netherlands
CCTCC	China Center for Type Culture Collection China
CCY	Culture Collection of Yeasts Slovakia
CECT	Colección Española de Cultivos Tipo Spain
CGMCC	China General Microbiological Culture Collection Center China
DSMZ	Deutsche Sammlung von Mikroorganismen und Zellkulturen Germany
ECACC	European Collection of Cell Cultures United Kingdom
IBFM-VKM	Russian Collection of Microorganisms Russian Federation
IMI	CABI Bioscience UK Centre (formerly: International Mycological Institute) United Kingdom
KRIBB	Korean Collection for Type Cultures Korea
MSCL	Microbial Strain Collection of Latvia Latvia
NBIMCC	National Bank for Industrial Microorganisms and Cell Cultures Bulgaria
NCAIM	National Collection of Agricultural and Industrial Microorganisms Hungary
NCIMB	National Collection of Industrial and Marine Bacteria Limited United Kingdom
NCYC	National Collection of Yeast Cultures United Kingdom
NIBH	National Institute of Bioscience and Human-Technology Japan
NRRL	Agricultural Research Service Culture Collection United States of America